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CHEST

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VISIT...

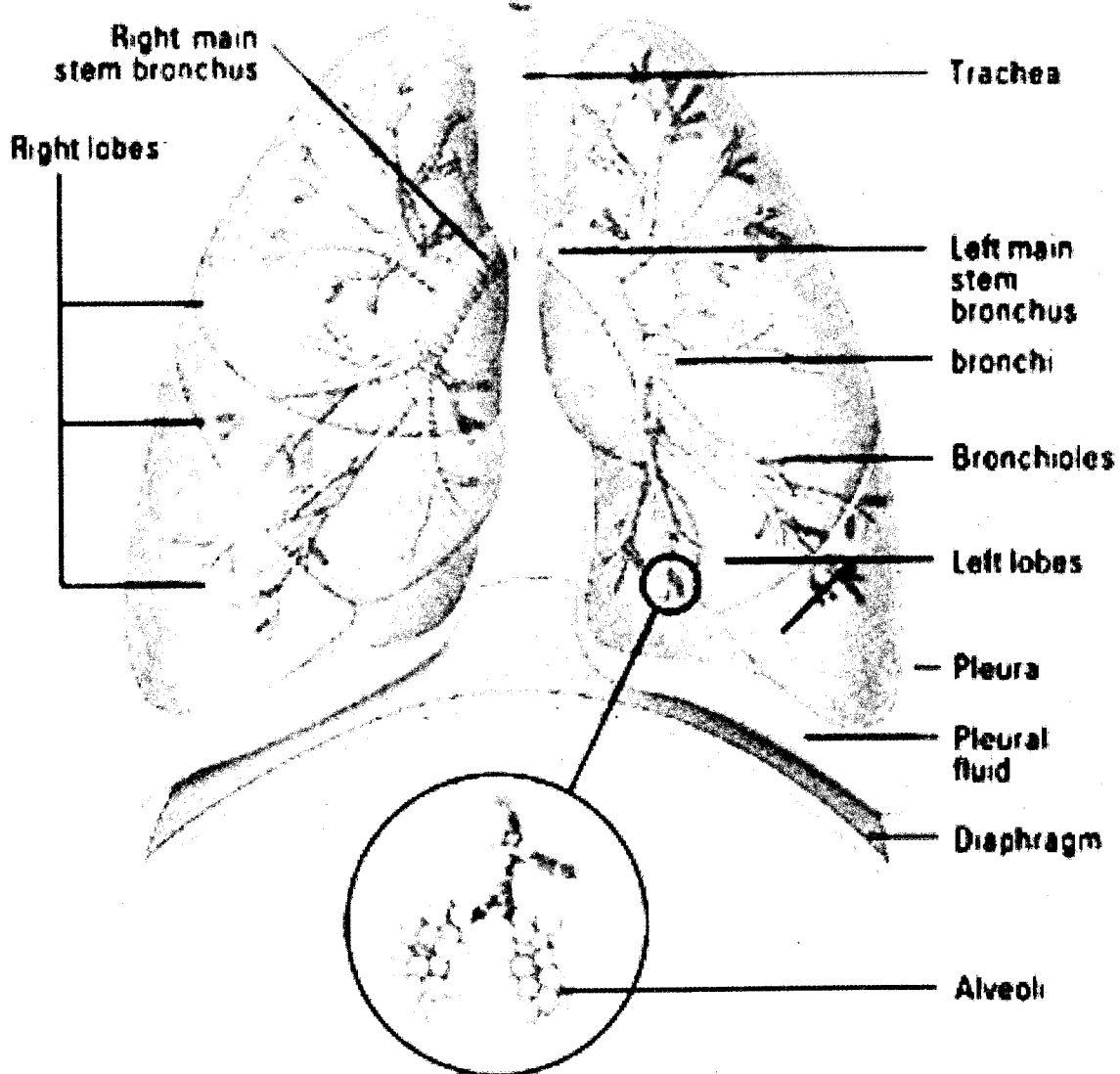
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“ Half of what you are taught as medical students will in 10 years prove to be wrong; and the problem is that none of your teachers knows which half ”

Dr. Sydney Burwell [1956]

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INTRODUCTION

CLASSIFICATION OF CHEST DISEASES

1. BRONCHIAL DISEASES:

- Bronchitis (*acute & chronic*).
- Bronchial asthma.
- Bronchiectasis.
- Bronchogenic carcinoma.

2. PARENCHYMATOUS LUNG DISEASES:

- Consolidation (*pneumonia*).
- Cavitation (*lung abscess*).
- Collapse.
- Fibrosis.
- Emphysema.
- TB.

3. PLEURAL DISEASES:

- Pleurisy.
- Pleural effusion.
- Pneumothorax.
- Hydropneumothorax.

4. MEDIASTINAL DISEASES.

5. DIAPHRAGMATIC DISEASES.

6. CHEST WALL DISEASES.

CHEST SYMPTOMS

- **COUGH**
- **HEMOPTYSIS**
- **CHEST PAIN**
- **DYSPNEA**

COUGH

DEFINITION

- **Cough** is an explosive expiration that provides a normal protective mechanism for clearing the tracheo-bronchial tree of: secretions & foreign material.
- It is the most common symptom of chest diseases.

ETIOLOGY

I. **Reflex cough:** (due to irritation of cough receptors)

A. **Respiratory causes:**

1. Airway diseases:

- **Inflammation:** Pharyngitis, Laryngitis,
BRONCHITIS, **BRONCHIECTASIS**.
- **Infiltration:** Sarcoidosis, **BR. CARCINOMA**.
- **Constriction:** **COPD**, **BR. ASTHMA**.
- **Compression:** Mediastinal masses, LN, AA (**Brassy cough**).

2. Parenchymatous lung diseases:

- Pneumonia, Lung abscess, Fibrosis, TB.

3. Pleural diseases:

- Pleurisy, Pleural effusion, Pneumothorax, Hydropneumothorax.

B. **Extra-respiratory causes:**

1. **Cardiovascular diseases:**

- Pulmonary congestion: Left – sided heart failure.
- Pulmonary embolism.

2. **Other causes:**

- Abdominal causes: Subphrenic abscess, GORD.
- DRUGS: ACE – I.

II. Central cough: (due to stimulation of the cough center)

- Brain tumours, Encephalitis, CVS.

III. Psychogenic (Hysterical) cough:

- Usually: dry cough in young neurotic females.

APPROACH TO THE PATIENT

1. Is the cough ACUTE or CHRONIC ??

- ACUTE (< 3 weeks): e.g. Pneumonia, Pulmonary embolism.
- CHRONIC (> 3 weeks): e.g. COPD, GORD.

2. Is the cough DRY or PRODUCTIVE ??

- DRY: e.g. Pleurisy, Psychogenic, DRUG (ACE – I).
- PRODUCTIVE: e.g. Chronic bronchitis, Bronchiectasis, Lung abscess.

3. Is there PERIODICITY ?? (DIURNAL or SEASONAL)

- DIURNAL
 - (Early morning): e.g. Bronchitis, Br. asthma, Bronchiectasis.
 - (Nocturnal): e.g. Cardiac asthma.
- SEASONAL (winter): e.g. Bronchitis, Br. asthma, Bronchiectasis.

4. Is there associated WHEEZING ??

- GENERALISED: e.g. Bronchitis, Br. asthma, Bronchiectasis, COPD.
- LOCALISED: e.g. Br. carcinoma.

5. Is the patient taking an ACE – I ??

COMPLICATIONS

*

I. Thoracic

1. Rupture of a pulmonary *bleb* or *bulla* → Pneumothorax.
2. Rupture of bronchial varices → Hemoptysis.
3. Rupture of an aneurysm.
4. Stress fracture of a rib.

II. Extrathoracic

1. Increased intra-abdominal pressure:

- Hernia.
- Prolapse: *rectal or utero – vaginal.*
- Stress incontinence of: *urine or stools.*

2. Increased intra-ocular pressure:

- Retinal & subconjunctival hemorrhages.
- Retinal detachment.
- Puffiness of the eye lids.

3. Increased intra-cranial pressure:

- Rupture of an aneurysm → SAH.
- Cough syncope.

4. OTHERS:

- Insomnia.
- Cough – induced vomiting.

* You have a cough? Go home tonight, take a whole bottle of Picolax;
a potent laxative, tomorrow you'll be afraid to cough... ~ **Pearl Williams**

HEMOPTYSIS

DEFINITION

- Coughing of blood originating from: below the vocal cords.
- Bleeding originating from above the vocal cords is known as: false hemoptysis.
- Hemoptysis may be: *frank or blood tinged*.

ETIOLOGY

(1) Respiratory causes:

A. Laryngeal causes:

- Inflammation.
- Tumours.

B. Tracheo-bronchial causes:

- Acute **B**ronchitis. (the most common cause)
- **B**ronchiectasis.
- **B**ronchial carcinoma.
- **B**ronchial adenoma.

C. Pulmonary causes:

- Pulmonary TB.
- Pulmonary embolism.
- Pneumonia.
- Lung abscess.
- Goodpasture syndrome.

(2) Cardiovascular causes:

- Pulmonary congestion, e.g. MS & acute pulmonary oedema.
- Pulmonary infection.
- Pulmonary infraction.
- Rupture of bronchial varices.
- Rupture of aortic aneurysm.

(3) Systemic diseases:

Hemorrhagic blood diseases, e.g.

- Hemophilia.
- Purpura.

MANAGEMENT OF HEMOPTYSIS

I. Diagnosis:

1 Differentiation between hemoptysis & hematemesis:

	Hemoptysis	Hematemesis
<i>Past history</i>	Chest disease	GIT disease
<i>The attack</i>	Cough	Vomiting
<i>Blood</i>	Bright red, frothy	Dark red, food particles
<i>After the attack</i>	Streaked sputum	Melena
<i>Examination</i>	Chest signs	Abdominal signs
<i>Investigations</i>	Chest or heart disease	GIT disease

2 Exclusion of false hemoptysis:

- Examination of the upper respiratory tract usually reveals the cause.

3 Detection of the cause of hemoptysis:

A) Clinical picture:

- Symptoms & Signs.

B) Investigations:

- Chest imaging: CXR, CT.
- Cardiac investigations: ECG, Echocardiography.
- Laboratory investigations: CBC, Bleeding profile, sputum analysis.
- BRONCHOSCOPY.

II. Treatment:

1. Treatment of the cause.
2. Cases of massive hemoptysis require:
 - *Hospitalization.*
 - *Sedation.*
 - *Blood transfusion & anti-shock measures.*

CHEST PAIN

ETIOLOGY

I. Cardiovascular causes:

- Myocardium: CAD (*angina or infarction*).
- Pericardium: Pericarditis or pericardial effusion.
- Endocardium: Mitral valve prolapse.
- Aorta Aortic aneurysm & Aortic dissection.
- Pulmonary: Pulmonary embolism & Pulmonary infarction.
- Pain of cardiac neurosis.
- Huge cardiomegaly.

II. Respiratory causes:

- Pleural disease: *pleurisy, pleural effusion, pneumothorax, hydropneumothorax.*
- Pulmonary disease extending to the pleura , e.g. *pneumonia & lung abscess.*
- Acute massive lung collapse.

III. Chest wall causes:

- Skin: wounds.
- Breast: mastitis, tumour.
- Ribs: osteomyelitis, tumour, fracture, Tietze syndrome.
- Intercostal muscles: myositis, muscle strain (from severe cough).
- Intercostal nerves: nerve root pain (herpes zoster).

IV. Mediastinal causes:

- Tumours, LN, Mediastinitis.

V. GIT:

- GORD, peptic ulcer, cholecystitis.

CAUSES OF ACUTE CHEST PAIN

- (1) MYOCARDIUM: angina pectoris & acute myocardial infarction.
- (2) PERICARDIUM: acute pericarditis.
- (3) ENDOCARDIUM: mitral valve prolapse.
- (4) AORTA: dissecting aneurysm of the aorta.
- (5) PULMONARY: massive pulmonary embolism & pulmonary infarction.
- (6) CARDIAC NEUROSIS.

- (7) Pleural disease: acute pleurisy & pneumothorax.
- (8) Lung disease: acute massive lung collapse.

- (9) Musculo-skeletal disorders: Tietze syndrome.

- (10) Nerve root pain: Herpetic neuralgia.

- (11) GIT: GORD, peptic ulcer, cholecystitis.

DYSYPNEA

ETIOLOGY

1. Cardiovascular diseases

1. **P**ulmonary congestion: *Left – sided heart failure.*
2. **P**ulmonary embolism.
3. **P**ericardial effusion.

2. Chest diseases

1. Laryngeal:
 - Foreign body, Tumours.
2. Tracheo-bronchial:
 - **B**ronchitis, **Br**. asthma, **B**ronchiectasis, COPD.
3. Lung:
 - Consolidation, Collapse.
 - Fibrosis (pulmonary, ILD).
4. Pleural:
 - Pleurisy, pleural effusion, pneumothorax, hydropneumothorax.
5. Chest wall:
 - Chest deformities, scleroderma, marked obesity (*Pick syndrome*).

3. Abdominal diseases

- Abdominal distension, **e.g.** marked ascites.

4. General diseases

- Anemia.
- Hemorrhage & shock.
- Acidosis.

5. Neurological diseases

1. Diaphragmatic paralysis.

2. Disorders of neuromuscular apparatus:

- CNS: Head injury, CVS, Drugs (*opiates & barbiturates*).
- AHCs: MND, Poliomyelitis.
- Peripheral nerve: Polyneuropathy, **e.g.** GBS.
- NMJ: Myasthenia gravis.
- Muscle: Myopathies.

6. Psychogenic (Hysterical) dyspnea.

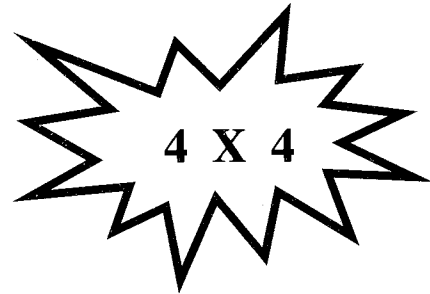
CAUSES OF ACUTE DYSPNEA

1. **Acute** massive myocardial infarction, (Acute LVF).

2. **Acute** pulmonary embolism.

3. **Acute** massive lung collapse.

4. **P**neumothorax (Tension).



5. **P**neumonia.

6. **P**leurisy.

7. *Bronchus*: Bronchial asthma.

8. *Larynx*: Inhaled FB, laryngeal spasm, laryngeal oedema.

9. **H**emorrhage, shock, acidosis.

10. **H**ysterical.

CHEST EXAMINATION

INSPECTION

1. Shape:

1. Symmetrical:

- Barrel chest: emphysema.

2. Asymmetrical:

- Unilateral bulge: pleural effusion, pneumothorax.
- Unilateral retraction: lung collapse, lung fibrosis.

2. Respiratory movements:

- In different chest diseases, respiratory movements are limited.

PALPATION

1. Trachea:

- To assess whether the trachea is **central** or **shifted** to one side:
 - Shift to the same side of the disease:
Occurs in the same causes of: unilateral retraction.
 - Shift to the opposite side of the disease:
Occurs in the same causes of: unilateral bulge.

2. Tactile Vocal Fremitus (TVF):

- Causes of increased TVF:
 - Consolidation, e.g. pneumonia.
 - Cavitation, e.g. lung abscess.
 - Cavitation surrounded by consolidation, e.g. bronchiectasis.
- Causes of decreased TVF:
 - Almost all other chest diseases.

PERCUSSION

Percussion notes in the chest	
Note	Disease
<i>Resonance</i>	Normal
<i>Hyper-resonance</i>	Hyperinflation as in asthma & emphysema Pneumothorax Very thin people
<i>Tympanitic resonance</i>	Tension pneumothorax
<i>Dullness</i>	Consolidation Cavitation Collapse Fibrosis
<i>Stony dullness</i>	Pleural effusion

Causes of Dullness over the Base of the Right lung:

1. Supra-diaphragmatic causes:

- Pleural disease: *pleural effusion, hydropneumothorax.*
- Basal lung disease: *consolidation, cavitation, collapse, fibrosis, bronchiectasis.*
- Heart disease: *huge pericardial effusion.*

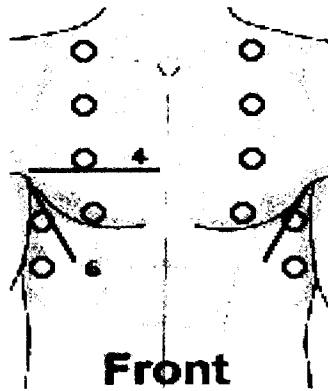
2. Diaphragmatic paralysis.

3. Infra-diaphragmatic causes:

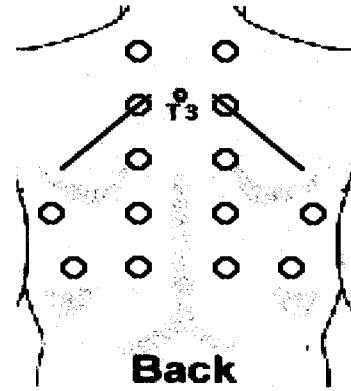
- *Acute liver abscess.*
- *Subphrenic abscess.*
- *Marked ascites.*
- *Pregnancy.*
- *Huge abdominal mass.*

4. Chest wall diseases:

e.g. tumours.



Points for:
Percussion
&
Auscultation



AUSCULTATION

I. BREATH SOUNDS

A) Types

1. Normal Vesicular Breathing:

- It is heard normally in: NORMAL persons.

2. Vesicular Breathing with prolonged expiration:

- It is characterized by: prolonged expiration.
- It is heard in: BRONCHIAL NARROWING.

3. Bronchial Breathing:

- It is characterized by: hollow sound (due to good conduction).
- It is heard in: CONSOLIDATION, CAVITATION.
- It is confirmed by: *bronchophony, aegophony, whispering pectoriloquy.*

B) Intensity

1. Decreased:

- Physiological: overweight persons.
- Pathological: collapse, fibrosis, pl. eff, pneumothorax, emphysema.

2. Increased:

- Physiological: very thin chest wall.
- Pathological: causes of bronchial breathing.

II. ADDITIONAL SOUNDS

A) Crepitations (*Crackles or Rales*)

Definition

- These are interrupted (non-continuous) sounds produced by:
 - o Passage of air through fluid in the respiratory passages, OR:
 - o Pulmonary fibrosis.

Types

- a) Fine:
 - Character: **like the sound of rolling a tuft of your hair between your fingers near your ear.**
 - Heard in: **LVF (basal & bilateral), TB (apical), Early Pneumonia.**
- b) Medium-sized: “Consonating or Non-consonating”
 - Character: **like the sound of a crack.**
 - Heard in: **Bronchiectasis, Lung abscess, Pneumonia, Fibrosis.**
- c) Coarse:
 - Character: **like the sound of loud gurgling & bubbling.**
 - Heard in: **Bronchiectasis, Lung abscess, Pulmonary oedema.**

Timing

- They are usually: **INSPIRATORY.**

Site

- o Localized: e.g. simple secretion, FB, tumour.
- o Generalized: e.g. pulmonary oedema.
- o Bilateral & Basal: e.g. LVF (fine), bronchiectasis (medium or coarse).
- o Kronig's isthmus: e.g. TB fibrosis.

Persistence after cough

- If you hear crepitations, ask the patient to cough & then auscultate again:
 - o If sounds persist = organic pathological lesion.
 - o If sounds disappear: = simple secretion.

B) Wheezes

(*Rhonchi*)

Definition

- These are continuous sounds produced by:
 - o Passage of air through the narrow bronchi e.g. COPD, Br. asthma.

Types

- a) Sibilant: high pitched due to narrowing of the SMALL bronchi.
- b) Sonorous: low pitched due to narrowing of the BIG bronchi.

Timing

- They are usually: EXPIRATORY.
- In severe obstruction: they may be heard also INSPIRATORY.

Site

- o Localized: e.g. simple secretion, FB, tumour.
- o Generalized: e.g. COPD, bronchial asthma.
- o Kronig's isthmus: e.g. Pancoast tumour.

Persistence after cough

- If you hear wheezes, ask the patient to cough & then auscultate again:
 - o If sounds persist = organic pathological lesion.
 - o If sounds disappear: = simple secretion.

C) Pleural rub

(see later).

Despign sign

- Normally: on the back you hear BB till the 2nd dorsal spine in adults.
- + ve sign: on the back you hear BB below the 2nd dorsal spine in adults in the presence of enlarged mediastinal lymph nodes (they act as good conducting medium).
- Confirm by: vocal resonance (bronchophony) & whispering pectorliquy.
- Value: it indicates the presence of enlarged mediastinal lymph nodes.

Local signs of chest disease

Chest disease	<i>Inspection</i>		<i>Palpation</i>		<i>Percussion</i>	<i>Auscultation</i>	
	Shape	Movement	Trachea	TVF	Note	Breath sounds	Additional sounds
Pleurisy	Normal	Decreased	Central	Normal	Normal, tender	Decreased	Rub
Pleural Effusion	Bulge	Decreased	Opposite side	Decreased	Basal stony dullness	Decreased	-----
Pneumothorax	Bulge	Decreased	Opposite side	Decreased	Hyper-resonance	Decreased	-----
Hydropneumothorax	Bulge	Decreased	Opposite side	Decreased	Shifting dullness	Decreased	-----
Consolidation	Normal	Decreased	Central	Increased	Dullness	Bronchial	Crepitations
Cavitation	Normal	Decreased	Central	Increased	Dullness	Bronchial	Crepitations
Collapse	Retraction	Decreased	Same side	Decreased	Dullness	Decreased	-----
Fibrosis	Retraction	Decreased	Same side	Decreased	May be patchy dullness	Decreased	Crepitations
Emphysema	Barrel	Decreased	Central	Decreased	Hyperresonance	Decreased	Rhonchi, Crepitations
Chronic Bronchitis	Normal	Decreased	Central	Decreased	Normal	Prolonged expiration	Rhonchi

VIP table

DISEASES OF THE PLEURA

- | | |
|---|---|
| 1. Dry pleurisy: | <u>INFLAMMATION ONLY</u> of the pleura. |
| 2. Pleural effusion (Hydrothorax): | <u>FLUID</u> in the pleura. |
| 3. Pneumothorax: | <u>AIR</u> in the pleura. |
| 4. Hydropneumothorax: | <u>FLUID & AIR</u> in the pleura. |
| 5. Fibrothorax: | <u>FIBROSIS</u> of the pleura. |
| 6. Mesothelioma (rare): | <u>TUMOUR</u> of the pleura. |

DRY PLEURISY

ETIOLOGY

A) Primary Pleurisy:

1. **I**diopathic (probably viral: Coxsackie B or Echo virus): the most common cause
 - Disease: BORNHOLM DISEASE, or PLEURODYNIA.
 - Age: Children & young adults.
 - CP: Onset (Acute + fever), Duration (few days), Course (Recurrent).
2. **I**nfections: *Viral, Bacterial, TB.*
3. **I**nflammation: *FMF.*
4. **I**mmunological: *SLE, RA.*
5. **I**atrogenic: *INH, Hydralazine, Procainamide.*
6. **I**rradiation.
7. **R**enal failure.
8. **R**heumatic.
9. **P**ost-traumatic.
10. **P**ost-cardiotomy syndrome.
11. **M**yocardial infarction.
12. **M**alignant infiltration.

B) Secondary Pleurisy: (due to extension from surrounding structures)

1) Lung disease:

- INFECTIONS (*TB, Pneumonia, Lung abscess*), MALIGNANCY (*Bronchogenic carcinoma*).

2) Mediastinal disease:

- INFLAMMATION (*Pericarditis*), MALIGNANCY (*Lymphoma*).

3) Subdiaphragmatic:

- ABSCESS: *Amoebic liver abscess or Subphrenic abscess.*

4) Chest wall disease:

- OSTEOMYELITIS: *Sternum, Ribs or Vertebrae.*

CLINICAL PICTURE

Symptoms

1. Symptoms of the CAUSE.

2. GENERAL symptoms: e.g.

- *Fever, malaise, headache.*

3. LOCAL symptoms:

A) PLEURITIC CHEST PAIN (due to irritation of the parietal pleura)

- Character & Duration: Severe Stitching, Continuous.
- Site & Reference: usually localized BUT may radiate:
 1. In inflammation of the central part of the diaphragmatic pleura:
pain radiates to the shoulder through the phrenic nerve.
 2. In inflammation of the outer part of the pleura:
pain radiates to the upper abdomen through the lower intercostals nerves.
(*this may simulate acute abdomen*).
- Increases by: Inspiration, cough & movements of chest wall.
- Decreases by: Holding breath & lying on the affected side.
- Associated symptoms: May be pain of dry pericarditis.

B) DRY COUGH due to irritation of the pleura.

C) DYSPNEA: due to ↓↓ of respiratory movements or to underlying lung disease.

Signs

1. Signs of the CAUSE.

2. GENERAL signs: **e.g.**

- *Fever.*

3. LOCAL signs:

Inspection

- Shape: normal.
- Movement: decreased.

Palpation

- Trachea: central.
- TVF: normal.
- May be palpable pleural rub.

Percussion

- Normal note.
- Tenderness: on the painful site.

Auscultation

- Breath sounds: decreased.
- Additional sounds: “ PLEURAL RUB ”
 - *It is due to friction between the 2 layers of the rough inflamed pleura.*
 - Site: **L**ocalised (at the painful site).
 - Character: **L**oud, **L**eathery, **L**ow – pitched.
 - Increases by: deep breathing & by pressing the stethoscope against chest the wall.
 - Disappears: on holding breath.

Complications

- Pleural effusion.

INVESTIGATIONS

- They have a negligible role in diagnosis, as dry pleurisy is diagnosed essentially:
clinically



Pleuritic pain + *Pleural rub*

- Investigations of the CAUSE.

DIFFERENTIAL DIAGNOSIS

1. From other causes of: acute chest pain.
2. DD of the causes of: dry pleurisy.
3. DD of the causes of: acute abdomen.

TREATMENT

Symptomatic:

- Analgesics & Anti-inflammatory drugs for the pain.

Specific:

- Treatment of the cause.

ETIOLOGY

1. Serous effusion

(ACCUMULATION OF EXUDATE)

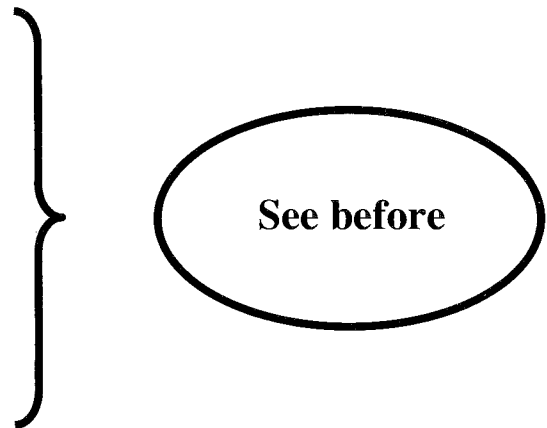
► It occurs in all conditions that cause dry pleurisy especially:

- **TB:** “the most common cause of pleural effusion”.
- Malignancy.

A) Primary pleural disease.

B) Secondary pleural disease:

- 1) Lung disease.
- 2) Mediastinal disease.
- 3) Subdiaphragmatic.
- 4) Chest wall disease.



2. Pyothorax

(ACCUMULATION OF PUS = EMPYEMA)

- Severe inflammation of the pleura due to:
Infection by pyogenic organisms, e.g. Staph. & Strept.

3. Hydrothorax

(ACCUMULATION OF TRANSUDATE)

- Hheart failure (RSHF & LSHF), pericardial effusion, CP.
- Hepatic failure.
- Hypoproteinemia, e.g. Nephrotic syndrome.
- Hypothyroidism.
- MEIG'S SYNDROME (Ovarian tumour, ascites, right pleural effusion).
- SVC OBSTRUCTION.

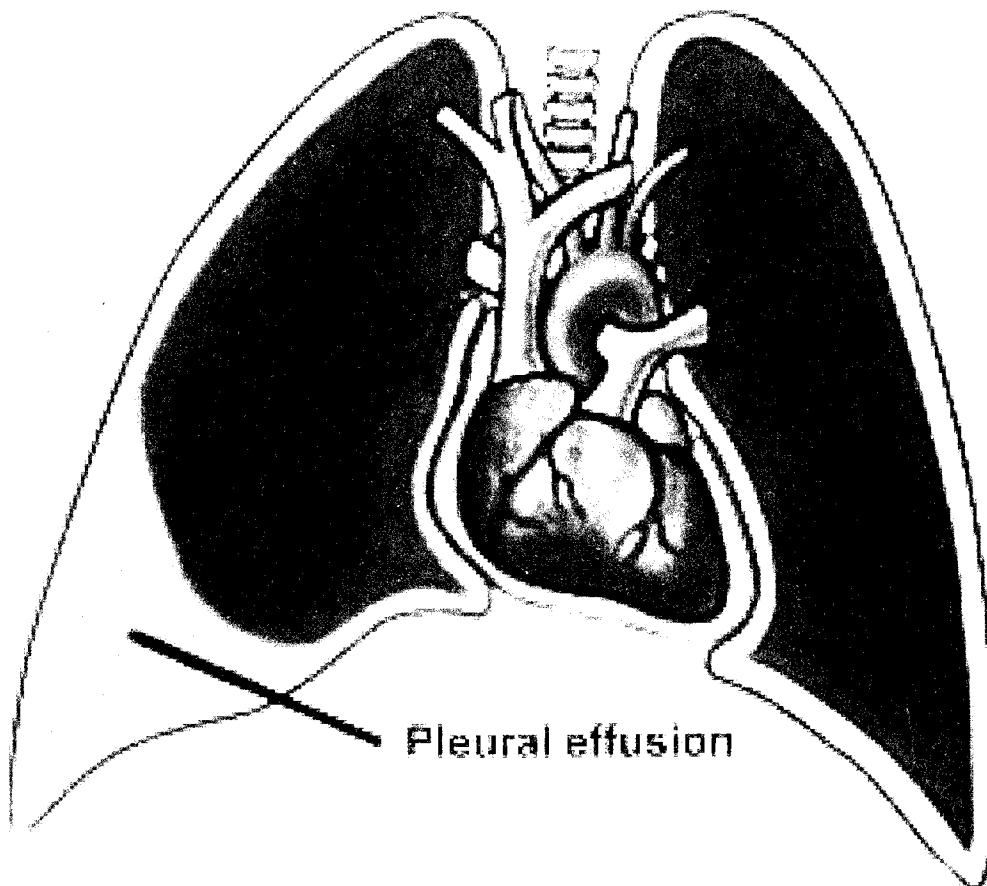
PLEURAL EFFUSION

DEFINITION

Abnormal accumulation of:

fluid in the pleural space:

- *Detected radiologically :* if more than 300 ml.
- *Detected clinically:* if more than 500 ml.



4. **Hemothorax**

(ACCUMULATION OF BLOOD)

1. Trauma: tapping of effusion & fracture rib.
2. TB.
3. Malignancy: “characteristics of malignant effusion”
 - *Massive, bloody.*
 - *Rapidly re-accumulates after aspiration, contains malignant cells.*
 - *May be: mediastinal shift to the same side (due to underlying collapse).*
4. Hemorrhagic blood diseases.

5. **Chylothorax**

(ACCUMULATION OF LYMPH)

- Obstruction: of thoracic duct.
- Rupture: of thoracic duct.

CLINICAL PICTURE

Symptoms

1. Symptoms of the cause: e.g. **TB toxemia.**
2. Symptoms due to effusion:
 - A) Small effusion: Asymptomatic.
 - B) Large effusion:
 - Dull aching chest pain.
 - Dyspnea.
 - Dry cough.

Signs

1. Signs of the CAUSE: e.g. TB.

2. LOCAL signs:

Inspection

- Shape: unilateral bulge in large effusion.
- Movement: decreased on the affected side.
- Littin's sign: negative.

Palpation

- Trachea & mediastinum:
 - a) Shift to the opposite side:
 - o *Small effusion:* no shift.
 - o *Moderate effusion:* shift of the apex to the opposite side.
 - o *Large effusion:* shift of the apex & trachea to the opposite side.
 - b) Shift to the same side:
 - o *Malignant effusion:* due to underlying lung collapse.
 - o *Chronic effusion:* due to pleural fibrosis.
- TVF: decreased on the affected side.

Percussion

- Dullness:
 - Basal stony dullness, with the upper level rising laterally to the axilla.
 - Grocco's triangle.
 - Garland's triangle.
- Resonance:
 - Skodiac resonance.

Auscultation

- Breath sounds: diminished.
- Additional sounds: PLEURAL RUB may be heard.

COMPLICATIONS

1. Infection: *empyema*.
2. Chronicity: *fibrosis* **or** *permanent lung collapse*.

INVESTIGATIONS

I. IMAGING:

1. CXR:

a) Free effusion:

- Homogenous opacity obliterating the CP angle & rising laterally:

- *Small effusion*: small opacity with no shift of apex or trachea.
- *Moderate effusion*: moderate opacity with shift of apex to opposite side.
- *Large effusion*: large opacity with shift of apex & trachea to opposite side.

b) Loculated effusion: *(especially in empyema)*

- Fluid may be loculated due to adhesions.
- Loculated fluid may be either:
 - 1) *At the periphery of the lung* *(encysted effusion)*:
 - Appears as a D – shaped capacity.
 - 2) *Within the fissures between the lobes* *(interlobar effusion)*:
 - Appears as a rounded or oval opacity that may disappear with diuretics: *phantom tumour* or *pseudo tumour*.

2. CT chest:

- Sensitive in detecting *small amounts* of pleural effusion.
- May detect *underlying lung disease* **e.g.** malignancy.

II. OTHER INVESTIGATIONS FOR THE CAUSE:

- THORACOCENTESIS: see later.
- Pleural biopsy: **e.g.** for TB or malignancy.
- Sputum examination: **e.g.** for TB or malignancy.
- Tuberculin test: **e.g.** for TB.
- Thoracoscopy: **e.g.** for malignancy.

THORACOCENTESIS:

(Aspiration of effusion)

- Indications of aspiration:

A] **Diagnostic:** "May be needed for diagnosis of the cause by analysis of the pleural fluid"

a) Features of exudate & transudate effusions:

	TRANSUDATE	EXUDATE
Proteins	< 3 gm %	> 3 gm %
Fluid protein / serum protein	< 0.5	> 0.5
Specific gravity	< 1016	> 1016
LDH	< 200 IU / L	> 200 IU / L
Fluid LDH / serum LDH	< 0.6	> 0.6
Cells (WBCs)	< 1000 / cmm	> 1000 / cmm

NB Characteristics of TB effusion:

1. Exudate: rich in Lymphocytes & RBCs.
2. TB bacilli can be detected by:
 - *Staining:* ZN stain.
 - *Culture:* Lowenstein-Jensen medium or BACTEC.
 - *Animal Innoculation:* Guinae pig.

b) Features of Pyothorax:

- The fluid is purulent & contains many pus cells.

c) Features of Hemothorax:

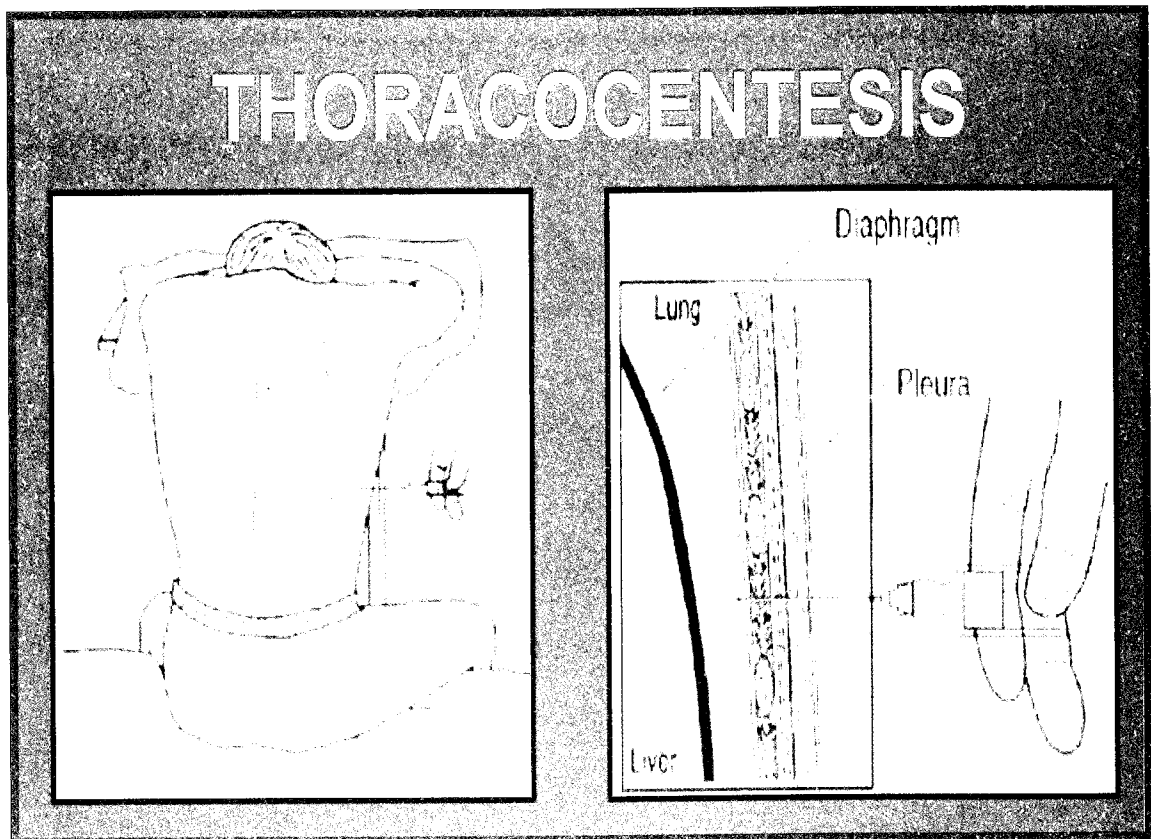
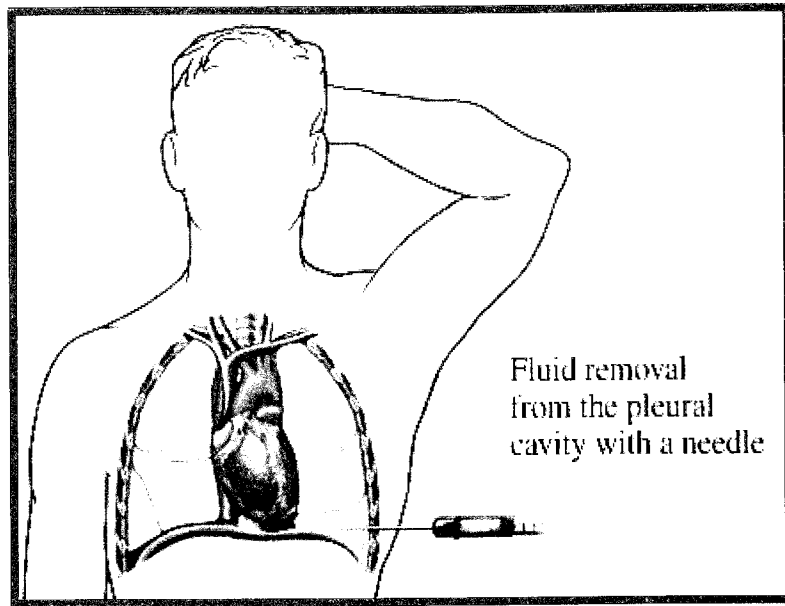
- The fluid is bloody & contains many RBCs.

d) Features of Chylothorax:

- The fluid is milky white & contains many fat,
clears on addition of ether & stains orange with: Sudan III.

B] **Therapeutic:**

(see later).

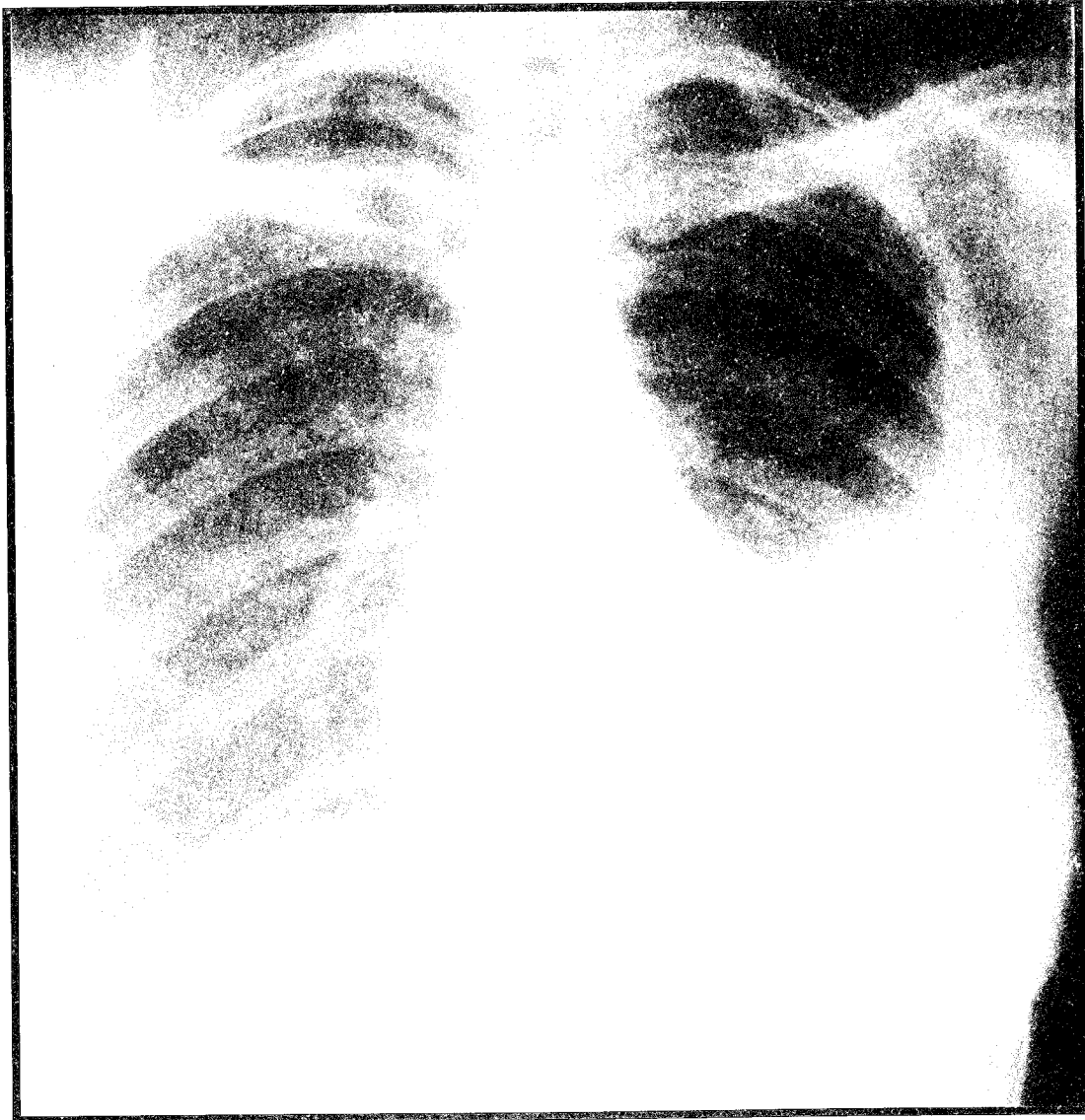


Mild left pleural effusion



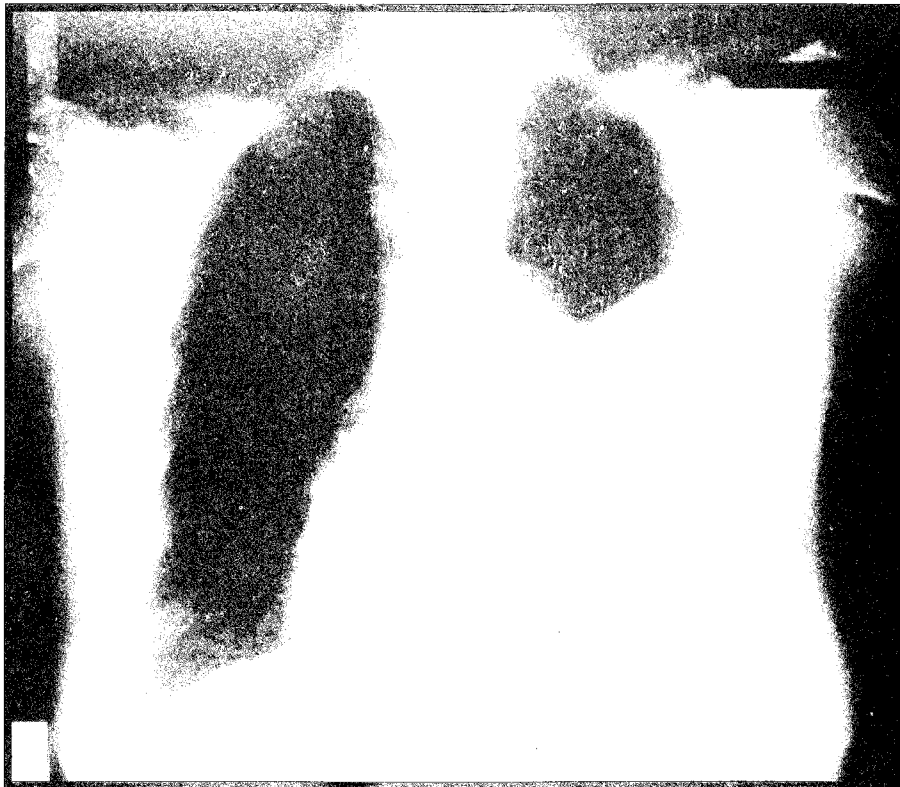
Mild right pleural effusion

Moderate left pleural effusion



Treat the patient, not the X-ray... ~ James M. Hunter

Massive left pleural effusion



Massive right pleural effusion

DIFFERENTIAL DIAGNOSIS

- 1) **Causes of:** “**syndrome of multiple negatives:**
 - *Pleural effusion, lung collapse, lung fibrosis.*
- 2) **From basal lung lesions:**
 - *Basal consolidation, collapse, fibrosis.*
- 3) **From subdiaphragmatic conditions:**
 - *Amoebic liver abscess & subphrenic abscess.*
 - *Tidal percussion may help in differentiation.*
- 4) **Differential diagnosis of the cause of effusion by:**
 - *Main Features of the cause.*
 - *Nature of pleural fluid.*

TREATMENT

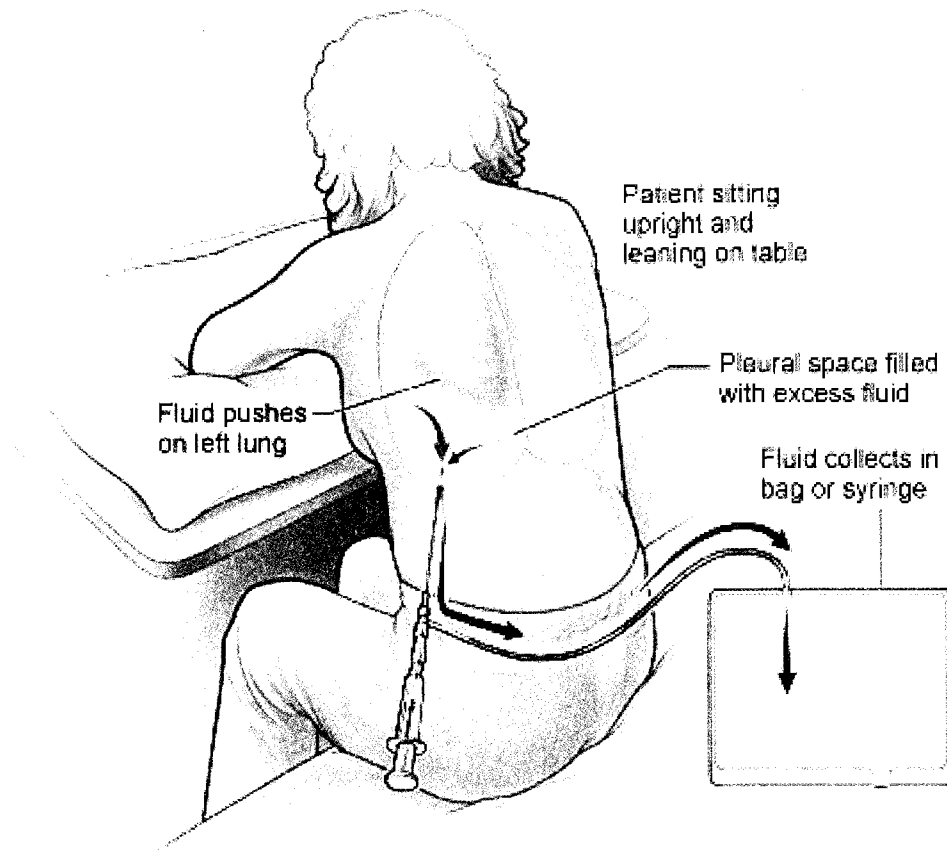
1. Treatment of the cause: **e.g.**

- a) Tuberculous effusion:
 - Anti – TB drugs.
 - Corticosteroids: *to ↓ inflammation & prevent fibrosis.*
- b) Malignant effusion:
 - Cytotoxic chemotherapy.
 - Pleural sclerosis: *by intrapleural injection of tetracycline.*

2. THORACOCENTESIS: (Aspiration of effusion)

INDICATIONS

1. Massive effusion: $\left\{ \begin{array}{l} \text{causing respiratory distress} \\ \text{or} \\ \text{reaching up to the second rib} \end{array} \right.$
2. Resistant effusion: not responding to treatment for **6 weeks**.
3. Effusion which becomes: ***secondary infected***.



CONTRAINDICATIONS

1. Bleeding tendency.
2. Uncooperative patient.

PRECAUTIONS

- Aspiration should be done slowly.
- Aspirated amount should not exceed: 1000 cc at a time.

BENEFITS

1. Relieves dyspnea.
2. Reduces pleural fibrosis & lung collapse.
3. Reduces the intrapleural pressure, so the lymphatics will open and absorb the remaining amount of fluid.

COMPLICATIONS

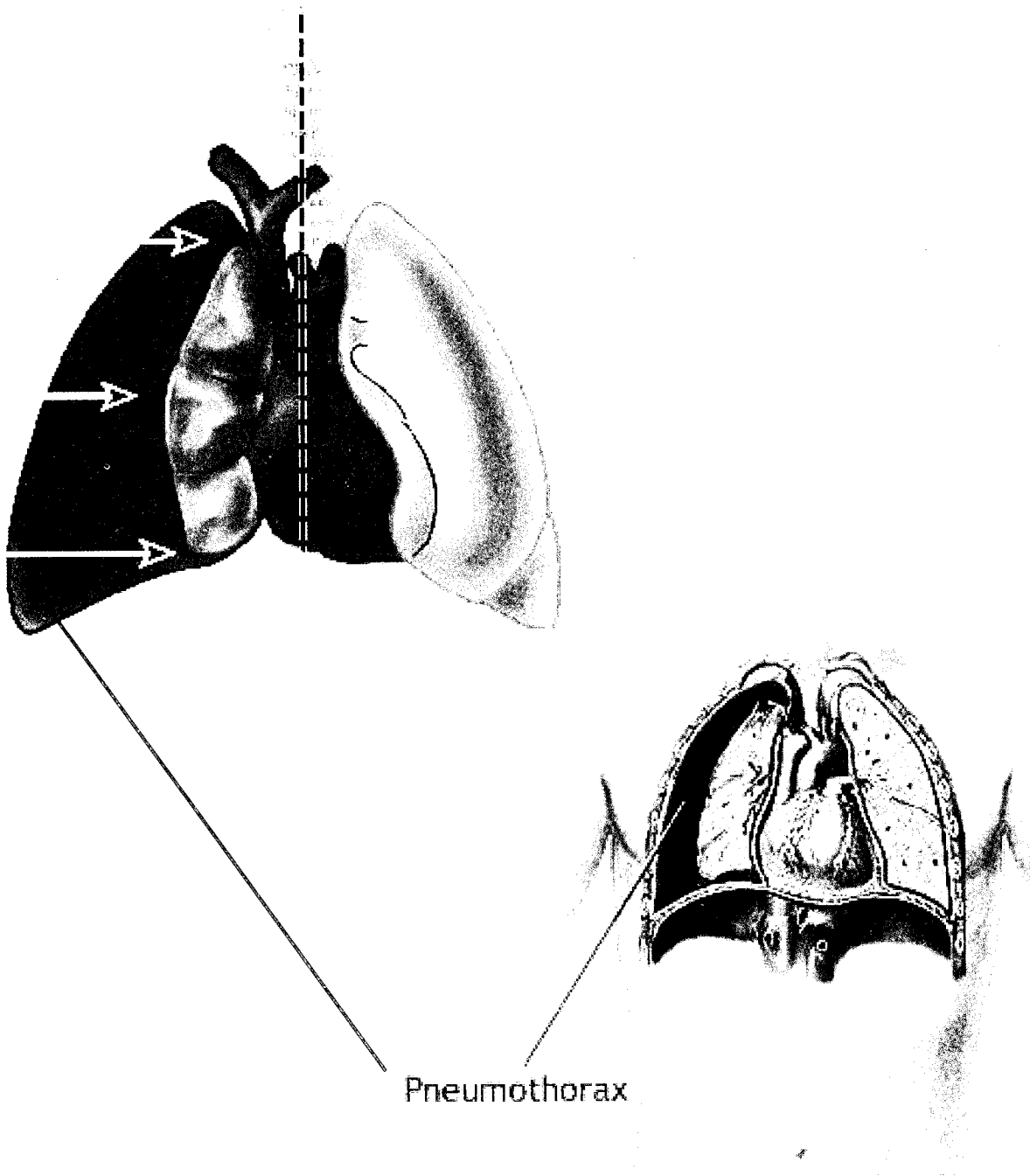
1. Neurogenic Shock:
 - Due to severe pain.
2. Acute pulmonary oedema:
 - Due to sudden expansion of the collapsed lung.
3. Introduction of:

- Air	→	<i>hydropneumothorax.</i>
- Blood	→	<i>hemothorax</i>
- Infection	→	<i>empyema.</i>
4. Injury:
 - Liver or spleen injury (rare complications).

PNEUMOTHORAX

DEFINITION

Abnormal accumulation of: *air* in the pleural space.



ETIOLOGY

1. Spontaneous pneumothorax (non-traumatic):

a. Primary (benign) spontaneous pneumothorax:

- Incidence: most common in males between 20 – 40 years especially smokers.
- Cause: **UNKNOWN,** there is no underlying disease:
 - It may be due to: unexplained rupture of a pulmonary bleb which is a localised collection of air most commonly in the apical zones.
 - It may be due to: a crack in a pleural scar resulting from a previous pneumonic patch.
 - It is spontaneously absorbed, but tends to be recurrent.

b. Secondary spontaneous pneumothorax:

- Incidence: related to the underlying disease.
- Cause: **KNOWN,** there is an underlying disease:

1. LUNG DISEASE:

- Rupture of emphysematous bullae: COPD.
- Rupture of a TB cavity: TB.
- Rupture of a lung cyst or abscess.
- SEVERE ASTHMA.

2. OESOPHAGEAL DISEASE: e.g. tumour, (rare).

3. INFRADIAPHRAGMATIC DISEASE:

- Rupture of a subphrenic abscess.

2. Traumatic pneumothorax:

a. Accidental pneumothorax:

- Wounds: penetrating chest injury.
- Invasive measures: e.g. surgery, thoracocentesis, pleural biopsy.
- Endoscopy: bronchoscopy, oesophagoscopy.
- MECHANICAL VENTILATION.

b. Artificial pneumothorax:

- Collapse therapy previously used for treatment of TB.

CLINICAL TYPES

1. Closed pneumothorax:

- The tear in the pleura is closed after the occurrence of pneumothorax.
- So the manifestations will: subside spontaneously.

2. Open pneumothorax:

- The tear remains open forming a fistula which communicates: the pleura with the outside atmosphere.
- So the manifestations will: remain stationary.

3. TENSION PNEUMOTHORAX:

- The tear is valve – like allowing air to enter the pleural sac during inspiration but preventing its escape during expiration.
- So the manifestations will be: progressive & may be life threatening.

CLINICAL PICTURE

Symptoms

1. Symptoms of the cause: e.g. COPD.

2. Symptoms due to pneumothorax:

A. In closed & open pneumothorax:

- Chest pain: *sudden, severe, tearing, increasing with inspiration.*
- Dyspnea: *acute onset.*
- Dry cough: *acute onset.*

B. In tension pneumothorax: “4 manifestations”

- Acute chest pain.
- Dyspnea (severe) & cyanosis.
- Acute RVF.
- Shock.

Signs

1. Signs of the CAUSE: e.g. COPD.

2. LOCAL signs:

Inspection

- Shape: unilateral bulge in: *tension type.*
- Movement: decreased on the affected side.

Palpation

- Trachea & mediastinum: shifted to the opposite side in: *tension type.*
- TVF: decreased on the affected side.

Percussion

- Hyper-resonance *or* tympanitic resonance.

Auscultation

- Breath sounds: diminished.
- Additional sounds: amphoric breathing in: *open & tension types.*

INVESTIGATIONS

1. CXR:

- a. Characteristically, there is the line of pleura forming the lung edge:
 - Outside this line:
Homogenous jet-black translucency devoid of lung markings (pneumothorax).
 - Inside this line:
The collapsed lung lies close to the mediastinum.
- b. The trachea & mediastinum: may be shifted to the opposite side.
- c. The cupola of the diaphragm: may be flattened or depressed.

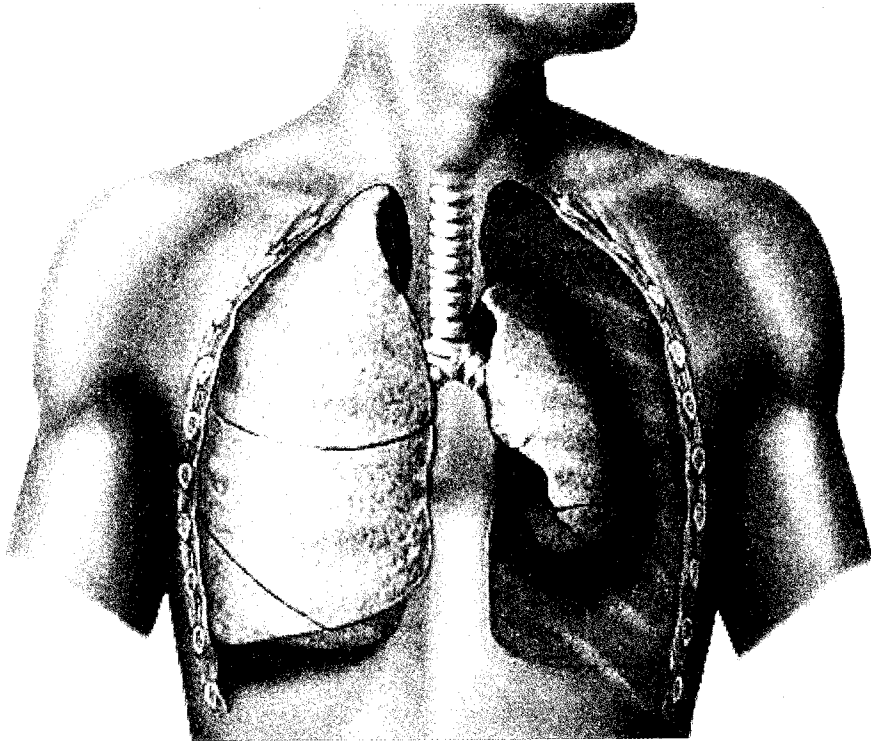
2. Intrapleural manometry:

For recording the intrapleural pressure:

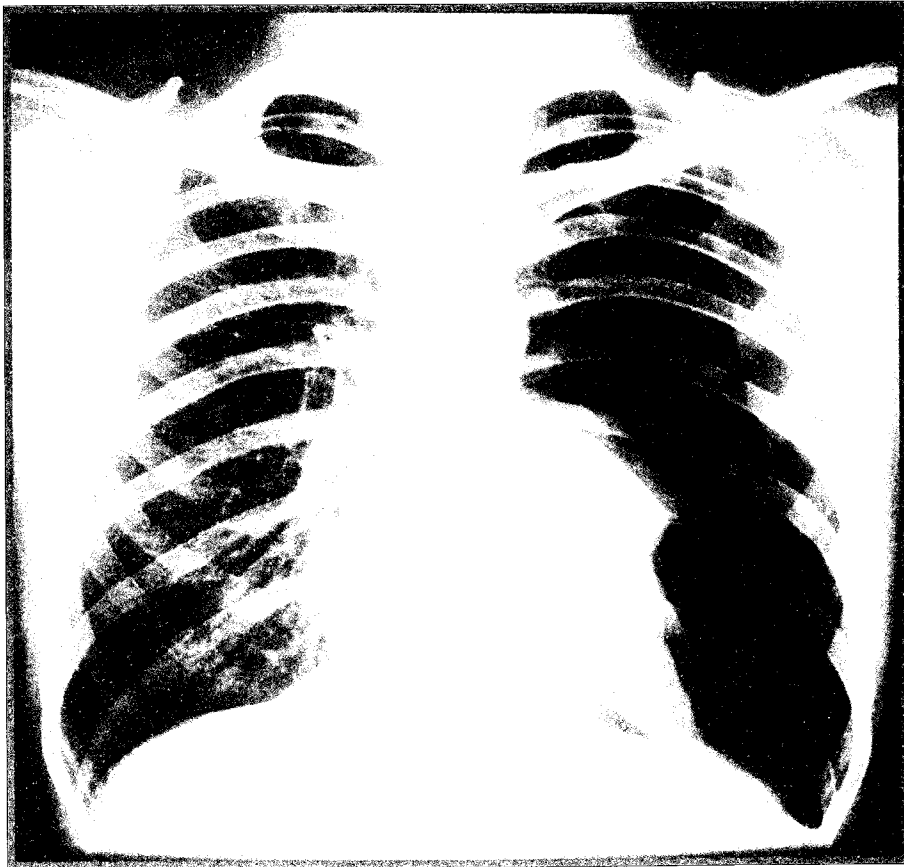
- a) In closed pneumothorax: *the pressure rises, but remains negative.*
- b) In open pneumothorax: *the pressure oscillates around zero.*
- c) In tension pneumothorax: *the pressure rapidly rises to become zero, and then becomes progressively positive.*

3. ABG:

- Hypoxia.

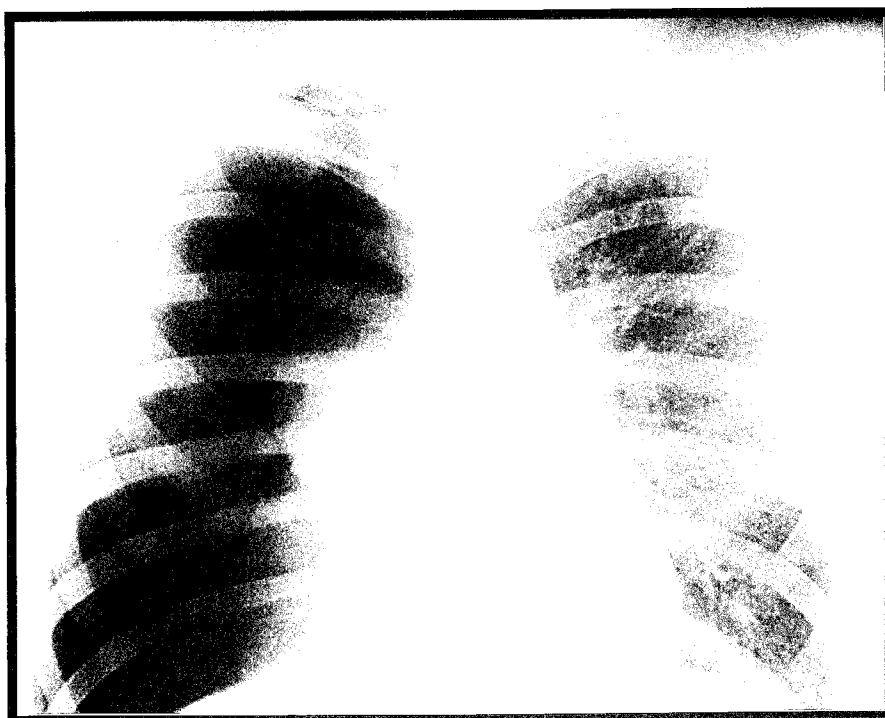


Left pneumothorax





Right pneumothorax



DIFFERENTIAL DIAGNOSIS

1. Differentiation of pneumothorax from:

- Other causes of: acute chest pain.
- Other causes of: acute dyspnea.
- EMPHYSEMA.

2. Differentiation of tension pneumothorax from:

- Other causes of: acute chest pain, dyspnea, acute RVF & Shock:
 - o Massive myocardial infarction.
 - o Massive pulmonary embolism.
 - o Massive lung collapse.

3. Differentiation between closed, open & tension pneumothorax:

	Closed	Open	Tension
1. <i>Dyspnea</i>	mild	mild	severe
2. <i>Cyanosis</i>	absent	absent	usually present
3. <i>Shock</i>	absent	absent	usually present
4. <i>Acute HF</i>	absent	absent	usually present
5. <i>Mediastinal shift</i>	absent	absent	usually present
6. <i>Amphoric breathing</i>	absent	present	present
7. <i>Intrapleural manometry</i>	See before		

TREATMENT

1. Conservative treatment:

- It is indicated in: primary spontaneous pneumothorax with:
 - o Mild symptoms.
 - o No increase in intrapleural pressure.
 - o Small pneumothorax (< 20 % of the hemithoracic volume).
- It consists of: bed rest & analgesics.
- Spontaneous absorption of air occurs allowing re-expansion of the collapsed lung.

2. Under water seal aspiration:

- It is indicated in:

- Severe symptoms.
- Severe increase in intrapleural pressure.
- Large pneumothorax (> 20 % of the hemithoracic volume).^{*}
- Tension pneumothorax.

3. Pleural sclerosis:

(production of pleural adhesions)

- It is indicated in: recurrent cases.
- It is done by intrapleural injection of: tetracycline.

4. Surgery:

(closure of the tear)

- It is indicated in:

- Failure of aspiration (lung fails to expand within 10 days).
- Recurrent pneumothorax.
- Bilateral pneumothorax.

5. Treatment of tension pneumothorax:

(medical emergency)

a) Life saving measure:

- Immediate under water seal aspiration: *to ↓ the intrapleural pressure rapidly.*

b) Treatment of the 4 manifestations:

- Immediate relief of pain: pethidine 50 mg IM.
- Immediate relief of dyspnea: oxygen inhalation.
- Immediate ttt of heart failure.
- Immediate ttt of shock.

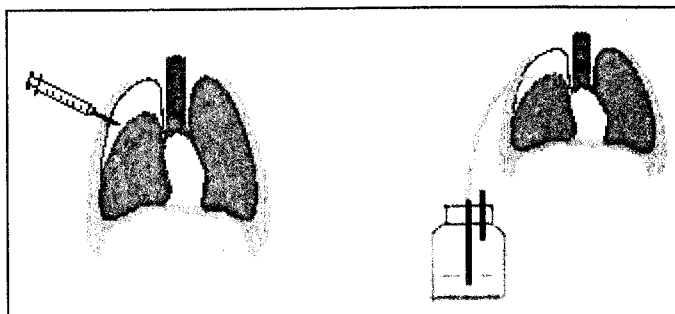
6. Treatment of the cause:

in secondary pneumothorax.

^{*} Thoracocentesis may be an alternative in large pneumothorax



< 20 % Pneumothorax:
Bed rest, analgesics

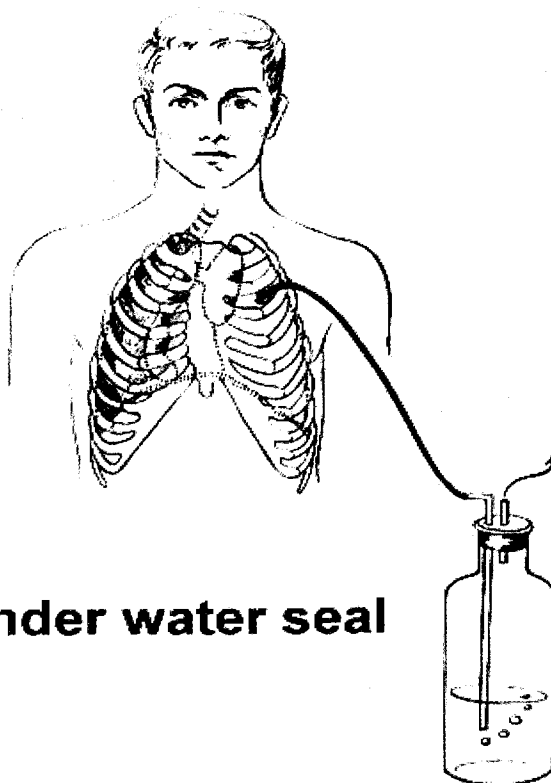


> 20 % Pneumothorax:
Thoracocentesis or under water seal

Therapeutic options

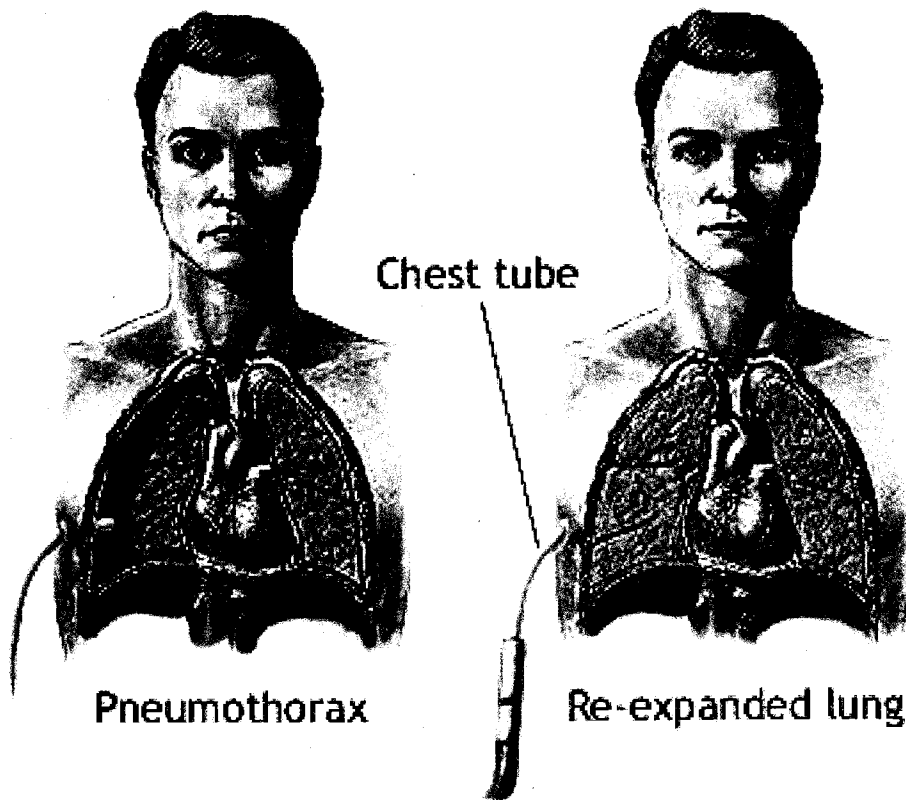
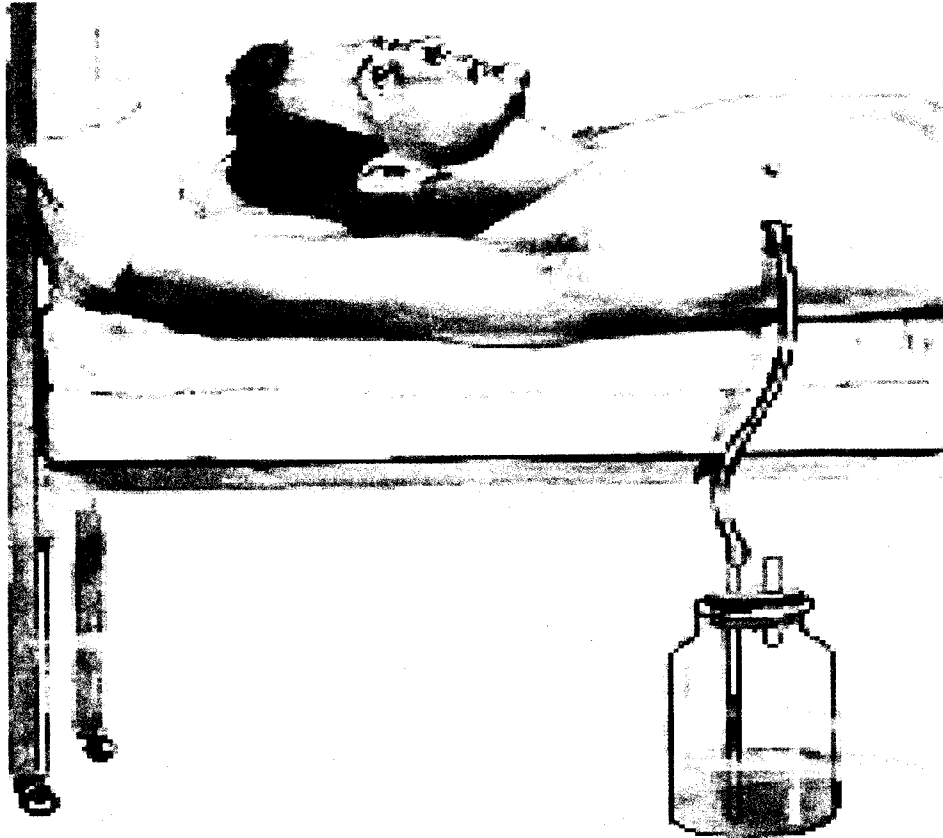
If the pneumothorax is less than 20 %:
the patient may need only bed rest & analgesics

If the pneumothorax is greater than 20 %:
air may be evacuated by thoracocentesis, or,
in more serious cases, by an under water seal



Under water seal

UNDER WATER SEAL



CLINICAL PICTURE

Symptoms

- Symptoms of: *the cause* e.g. **TB toxemia**.
- Chest symptoms: *chest pain, dyspnea, dry cough*.
- Symptoms of: *suppurative lung syndrome in cases with **bronchopleural fistula***.

Signs

1. Signs of the CAUSE: e.g. **TB**.
2. LOCAL signs:

Inspection

- Shape: unilateral bulge in: *large hydropneumothorax*.
- Movement: decreased on the affected side.

Palpation

- **T** rachea & mediastinum: shifted to the opposite side in: *large hydropneumothorax*.
- **T** VF: decreased on the affected side.

Percussion

- Stony dullness with horizontal upper level (below).
- Hyper-resonance or tympanic resonance (above).
- Shifting dullness: *is characteristic*.

Auscultation

- Breath sounds: diminished.

INVESTIGATIONS

1) CXR:

a. Characteristically, there is the line of pleura forming the lung edge:

- Outside this line:

- Below: homogeneous opacity obliterating the costophrenic angle, and has a horizontal upper level (air-fluid level).

- Above: homogeneous jet-black translucency devoid of lung markings.

- Inside this line:

- The collapsed lung lies close to the mediastinum.

b. The trachea & mediastinum: may be shifted to the opposite side.

c. The cupula of the diaphragm: may be flattened or depressed.

2) Aspiration of pleural fluid.

3) Methylene blue test:

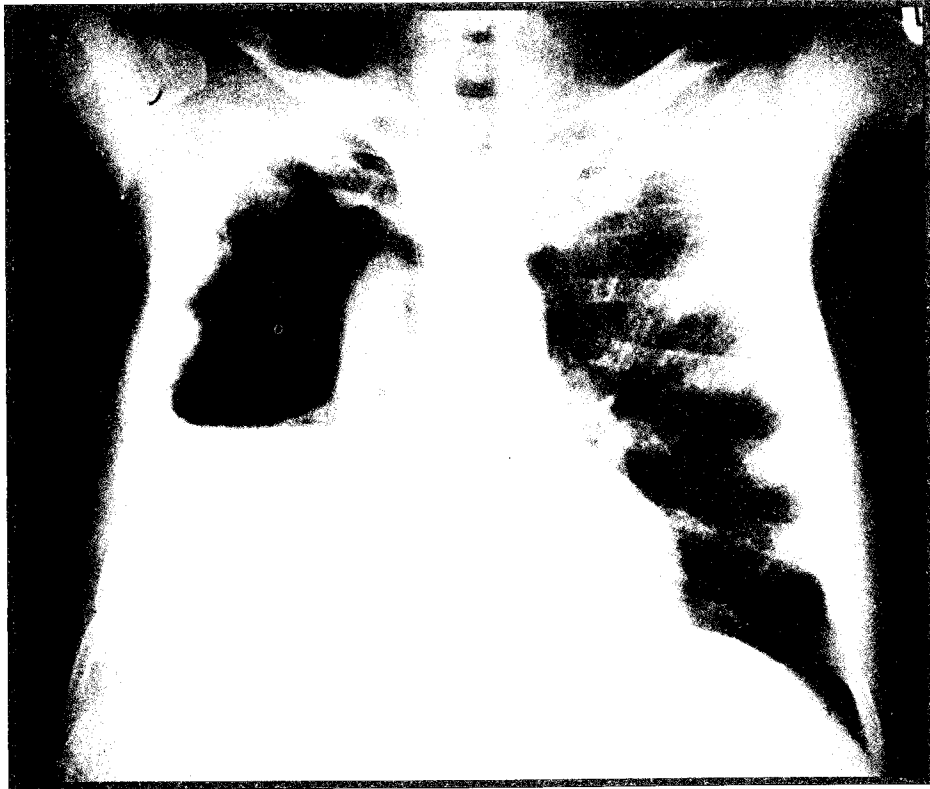
- In the presence of broncho-pleural fistula, Methylene blue injected in the pleura will appear in the sputum.

TREATMENT

1. Treatment of the cause.

2. Aspiration of fluid & air using an under water seal.

Right hydropneumothorax



Left hydropneumothorax

PNEUMONIA

DEFINITION

- INFLAMMATION of the lung: (usually acute)
 - Terminal airways.
 - Alveoli.
 - Interstitial tissue.
- It may be caused by: *infective & non – infective* factors.

CLASSIFICATION

A. Classification by LOCATION (Anatomical):

1. Lobar pneumonia:

- Localised inflammation of: a single entire lobe.

2. Bronchopneumonia:

- Diffuse bilateral patchy inflammation of: multiple lobules.
(affecting mainly: the alveoli adjacent to the bronchioles).

3. Interstitial pneumonia:

- Inflammation of: the interstitial tissue inbetween the alveoli.

B. Classification by CLINICAL PRESENTATION:

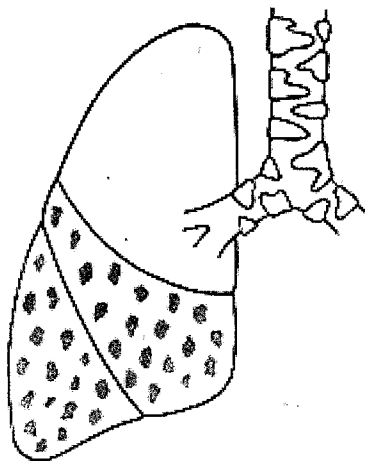
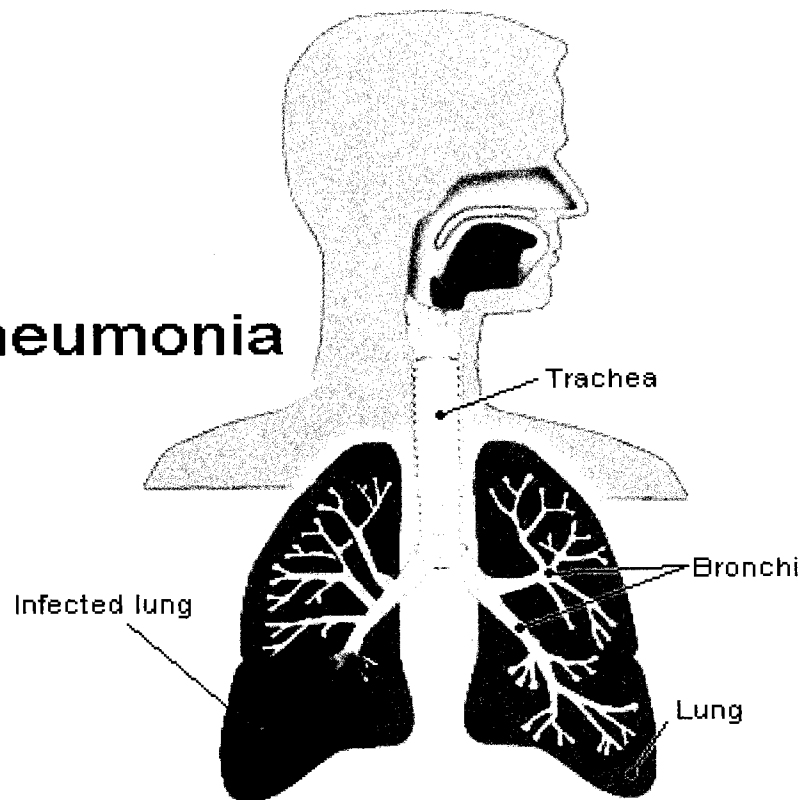
1. Acute pneumonia:

- It is the usual (common) type:
 - o Onset: acute.
 - o Duration: short (less than 3 weeks).
 - o Cause: the usual common organisms (see later).

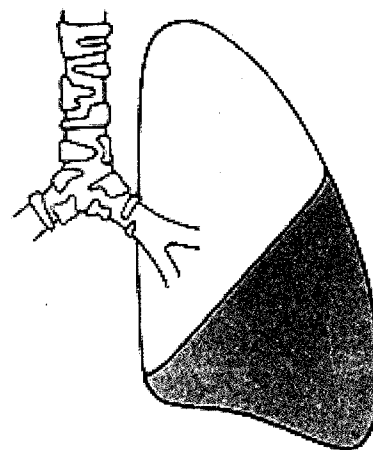
2. Chronic pneumonia:

- It is the unusual (rare) type:
 - o Onset: gradual.
 - o Duration: long (more than 3 weeks).
 - o Cause: mycobacteria, fungi, non – infective.

Pneumonia



Bronchopneumonia



Lobar pneumonia

C. Classification by ETIOLOGY:

I. INFECTIVE: [Most common]

1. The infecting organism:

- BACTERIA:
 - Gm + ve cocci: Strept. pneumoniae, Staph. aureus, St. pyogenes.
 - Gm - ve bacilli: H. influenzae, Klebsiella, Pseudomonas, Legionella.
 - Anaerobes.
 - Mycobacterium TB.
- Viruses:
 - Influenza virus, adenovirus, varicella, RSV, CMV.
- Mycoplasma.
- Chlamydia.
- Rickettsia.
- Fungi: e.g. Histoplasma, Candida.
- Protozoa: e.g. Pneumocystis carinii.
- Parasites: e.g. Filaria, Toxoplasma, Ascaris.

2. The mode of infection:

- Community – acquired pneumonia:
 - Strept. pneumoniae (pneumococcal pneumonia): most common.
 - Others: H. influenzae, Legionella, Mycoplasma, Chlamydia, Viruses.
- Hospital – acquired (Nosocomial) pneumonia:
 - Risk factors: Mechanical ventilators (VAP), IV cannulae.
 - Organisms:
 - Staph. aureus: most common.
 - Others: Klebsiella, Pseudomonas, Anaerobes.
- Aspiration pneumonia:
 - Risk factors: Stroke, Bulbar palsies, DCL, Anaesthesia, GORD.
 - Organisms:
 - Anaerobes: most common.
 - Others: Strept. pneumoniae, Staph. aureus, H. influenzae, Klebsiella.
- Pneumonia in the immunocompromised patient:
 - Risk factors: HIV, BM ↓, advanced malignancy, immunosupp. drugs.
 - Organisms:
 - Pneumocystis carinii: most common.
 - Others: Fungi, CMV, TB.

II. NON – INFECTIVE: [Least common]

- *Physical:* radiation pneumonitis.
- *Chemical:* chemical toxins such as pesticides.
- *Immunological:* SLE.
- *Allergic:* Loffler's syndrome (pulmonary eosinophilia).

LOBAR PNEUMONIA

CAUSATIVE ORGANISM

- It is usually caused by: Strept. pneumoniae.

PREDISPOSING FACTORS

- AGE: middle age.
- PRECEDING INFECTION: upper respiratory tract viral infection.
- ENVIRONMENT: cold weather, overcrowding.
- ↓↓ IMMUNITY: malnutrition, hyposplenism.

PATHOLOGY

A) LOCATION:

- Unilateral, usually involving one whole lobe.

B) LESION:

- Consolidation & acute pleurisy.
- The disease passes through 3 stages over 7 days:
 - a) Stage of congestion:
 - The alveoli are congested with: minimal exudate.
 - Air diminishes in the alveoli.
 - b) Stage of hepatization:
 - The alveoli are filled with: RBCs, WBCs fibrin, thick exudate.
 - c) Stage of resolution:
 - The exudate is **liquefied** by enzymatic activity & becomes copious & watery.
 - The exudate is then **cleared** by:
 - Macrophages: through the blood and lymph vessels, **or:**
 - Cough mechanism.

CLINICAL PICTURE

Symptoms

(Typical pneumonia)

A. General symptoms

- Fever:
 - Acute onset, high, associated with headache, malaise & rigors.
- Associated manifestations:
 - Somnolence & confusion: *especially in the elderly.*
 - Headache & convulsions: *especially in children.*

B. Chest symptoms

- Dyspnea.
- Pain:
 1. Pleuritic stitching.
 2. Upper abdominal pain & rigidity may occur in case of inflammation of the outer pleura & may simulate acute abdomen.
- Cough:
 1. Dry: *in the early stage.*
 2. Productive: *later*:
 - With rusty sputum: *during hepatization.*
(may be yellowish or greenish, with blood streaking).
 - With watery sputum: *during resolution.*

Signs

A. General signs

- Fever:
 - High continuous fever (40° C), lasts for about 7 days.
 - Resolves abruptly (by crisis).
- RR:
 - Tachypnea (40 / min).
- Face:
 - Pale & toxic.
- Lips:
 - Herpes simplex eruptions.

B. Chest signs (Signs of consolidation & pleurisy)

Inspection

- Shape: normal shape of the chest.
- Movements: limited on the affected side.

Palpation

- Trachea & mediastinum: central.
- TVF: increased.

Percussion

- Dullness: on the affected area (lobe), due to consolidation.
- Tenderness: on the affected area (lobe), due to pleurisy.

Auscultation

- Breath sound: bronchial breathing.

- Additional sounds: crepitations:

<u>Fine</u> :	early stage
<u>Medium sized</u> :	during hepatization
<u>Coarse</u> :	during resolution

- Pleural rub: is usually present.

COMPLICATIONS

A. General complications

- Toxic myocarditis: may lead to HF.
- Bacteremia: meningitis, peritonitis or suppurative arthritis.
- Septicemia: in severe cases may cause DIC, ARDS.

B. Chest complications

- Unresolving pneumonia (persisting more than 2 weeks).
- Lung abscess.
- PLEURA: *Pleural effusion, Empyema.*

UNRESOLVING PNEUMONIA

- **DEFINITION:** Pneumonia that persists more than 2 weeks.
- **CAUSES:**
 1. Inadequate treatment.
 2. Underlying lung disease **e.g.** bronchiectasis & bronchial carcinoma.
 3. TB pneumonia.
 4. Decreased immunity:
 - o **D**iabetes mellitus.
 - o **D**rugs: Corticosteroids & other immunosuppressives.
 - o **A**IDS.
 - o **M**alignancies, especially lymphomas.
 - o **M**alnutrition.

INVESTIGATIONS

I. IMAGING: **CXR**

- Homogenous opacity: unilateral, usually involving one whole lobe.
- Complication: **e.g.** pleural effusion, lung abscess.

II. LABORATORY INVESTIGATIONS:

1. **Sputum examination (C&S):**
 - Pneumococci appear as: Gm + ve diplococci.
2. **Blood picture:**
 - Leukocytosis: with shift to the left.
3. **Blood culture:**
 - Pneumococci: may be detected.
4. **ABG:**
 - May show: Hypoxia & Hypocapnia.
5. **INVESTIGATIONS FOR COMPLICATIONS:**
 - Culture of aspirated pleural fluid.

Lobar pneumonia



DIFFERENTIAL DIAGNOSIS

- Causes of: acute high fever with chest symptoms, e.g. acute lung abscess.
- Consolidation should be differentiated from:
 Collapse, fibrosis, pleural effusion.
- Differentiate between: lobar pneumonia & bronchopneumonia.
- FUO.

TREATMENT

1. General Treatment:

- Bed rest.
- Proper nutrition.

2. Specific Treatment: (antibiotics)

- Crystalline penicillin G: 1 million u / 6h IV (7 days).
- In allergy to penicillin:
 - *Erythromycin*: 500 mg / 6 h IV (7 days) **or**:
 - *Cephalosporins*.
- In resistant cases: antibiotics are given according to C & S.

3. Symptomatic Treatment:

- Analgesics & Antipyretics.
- For early dry cough: cough sedatives, e.g. codeine phosphate.
- For productive cough:
 - *Mucolytics*: **e.g.** Bromhexine.
 - *Expectorants*: **e.g.** Potassium iodide.
- Oxygen inhalation: in severe cases.

4. TREATMENT OF COMPLICATIONS:

- **e.g.** ttt of pleural effusion.

BRONCHOPNEUMONIA

CAUSATIVE ORGANISM

- BACTERIA:
 - Gm + ve cocci: *Staph. aureus*, *St. pyogenes*.
 - Gm - ve bacilli: *H. influenzae*, *Klebsiella*, *Pseudomonas*, *Legionella*.
 - Anaerobes.
 - Mycobacterium TB.
- Viruses:
 - Influenza virus, adenovirus, RSV, CMV.
- Mycoplasma.
- Chlamydia.
- Rickettsia.
- Fungi: e.g. *Histoplasma*, *Candida*.
- Protozoa: e.g. *Pneumocystis carinii*.
- Parasites: e.g. *Filaria*, *Toxoplasma*, *Ascaris*.

PREDISPOSING FACTORS

- AGE: *extremes of age* (children & elderly).
- UNDERLYING CHEST DISEASE: *e.g. chronic bronchitis*.
- ENVIRONMENT: *cold weather*, *overcrowding*.
- ↓↓ IMMUNITY: *malnutrition*, *hyposplenism*.
- HOSPITALIZED PATIENTS.

PATHOLOGY

A) LOCATION:

- Diffuse bilateral patchy inflammation of: *multiple lobules*.
(affecting mainly: the alveoli adjacent to the bronchioles).

B) LESION:

- Lobular consolidation & may be bronchiolitis & bronchitis.

DIAGNOSIS

Similar to lobar pneumonia with the following differences:

	Lobar Pneumonia	Bronchopneumonia
<i>Age</i>	Middle	Extremes
<i>Onset</i>	Acute	More gradual
<i>Offset</i>	By crisis	By lysis
<i>Duration</i>	1 week	2 weeks
<i>Pathology</i>	Lobar consolidation	Lobular consolidation & bronchitis
<i>Complications</i>	Less common	More common
<i>CXR</i>	Lobar consolidation	Bilateral patchy opacities

TREATMENT

- Same lines of treatment of Lobar pneumonia, **BUT:**
- Specific ttt (Antibiotics): depends on the causative organism (see later).

Special types of pneumonias

1. BACTERIAL

a) Staphylococcal bronchopneumonia:

- Commonly occurs in: hospitalized patients.
- Commonly follows: a viral illness.
- There is tendency to: ABSCESS FORMATION → empyema.
- May take a fatal course leading to death from Staph. septicemia.
- **Treatment:** Cloxacillin or Vancomycin.

b) Streptococcal bronchopneumonia:

- Characteristically associated with: MARKED TOXEMIA.
- **Treatment:** Penicillin G or Erythromycin.

c) Friedlander's pneumonia: (Klebsiella)

- Characteristically affects: APICAL ZONES (DD of apical lesions).
- There is tendency to: ABSCESS FORMATION → empyema.
- Characteristically there is: viscid, purulent, blood-stained sputum.
- **Treatment:** Aminoglycosides or Cephalosporins.

d) Legionnaire's disease: (Legionella pneumophila)

- Occurs in: outbreaks or sporadically.
- Spreads usually in: places with contaminated cooling systems.
- **Clinical picture:** [Multisystem affection]
 - *General:* gradual onset with fever & rigors.
 - *Chest:* cough (dry then productive) & dyspnea.
 - *GIT:* nausea, vomiting & watery diarrhea.
 - *Heart:* myocarditis.
 - *Neurological:* mental confusion.
 - *Renal:* ARF.
- **Investigations:**
 - *CXR:* Lobar consolidation or Bilateral patchy opacities.
 - *Sputum:* organism is detected with special stain: **Gimenez**.
 - *Serology:* Immunofluorescent antibody (IFA): **↑ Ab titre**.
- **Treatment:** **Clarithromycin** or **Ciprofloxacin**.

2. NON - BACTERIAL

a) Viral pneumonia:

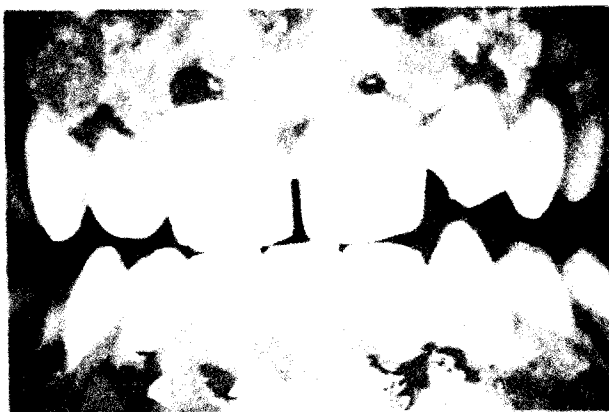
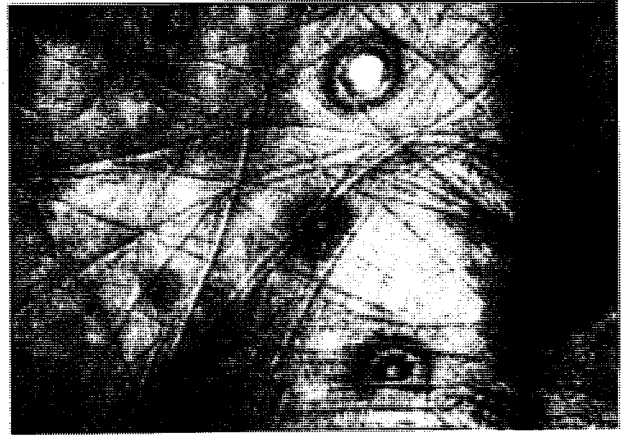
- The most common cause of pneumonia in: children.
- Causative organisms: Influenza virus, adenovirus, varicella, RSV, CMV.
- Clinical picture:
 - General: Flu – like symptoms & may be skin rash.
 - Chest: dry cough, dyspnea, few physical signs.
- Investigations:
 - CXR: may show bilateral patchy opacities.
 - Serology: antibodies to specific viruses.
- Treatment: Antiviral drugs: e.g. Ribavirin for RSV.

b) Atypical pneumonia:

- Causative organisms: MYCOPLASMA, chlamydia, rickettsiae.
- Clinical picture:
 - Onset:

more gradual onset with a rather mild fever
 - Chest:
 1. Cough (dry, may be productive) & dyspnea.
 2. Minimal physical signs on the chest (few crepitations).
 - Extrapulmonary:
 1. General: fatigue, headache, myalgias.
 2. Skin: erythema multiforme.
 3. Blood: AIHA (cold agglutinins).
 4. Neurological: meningitis & encephalitis.
- Investigations:
 - CXR: Severe abnormalities on CXR despite minimal physical chest signs:
“Bilateral patchy opacities or GGA”.
- Treatment: Clarithromycin or Tetracyclin.

Erythema Multiforme



WALKING PNEUMONIA

- An old term that was previously used to describe:
 - A clinically mild form of pneumonia.
 - Affected patients do not need hospitalization.
 - Causative organisms: MYCOPLASMA, chlamydia, rickettsiae.
(Atypical pneumonia)

c) Pneumocystis carinii pneumonia: (Protozoa)

- The most common opportunistic infection causing pneumonia in immunocompromised patients, especially: **HIV**.
- **Diagnosis:**
 - CXR: may show bilateral patchy opacities.
 - Detection of organism: *Bronchoscopy with BAL* **or** *open lung biopsy*.
- **Treatment:** **Co-trimoxazole** or **Pentamidine**.

LUNG ABSCESS

DEFINITION

- It is a localized **SUPPURATION** in the lung with cavity formation and fluid level, that is not due to TB.

ETIOLOGY

1. Primary (inhalation) lung abscess: *"the most common"*

- Risk factors:

- a) Inhalation of a specific material: **e.g.**
 - FB, vomitus (e.g. GORD).
- b) Absent cough reflex:
 - Stroke, Bulbar palsies, DCL, Anaesthesia.

- Causative organisms:

- Anaerobes.
- Gm +ve: Staph. aureus, Strept. pneumoniae.
- Gm – ve: Klebsiella, H. influenzae.

2. Secondary lung abscess:

A. Thoracic causes:

1] Lung disease:

- Pneumonia, esp. Staph. aureus, Klebsiella.
- Bronchiectasis.
- Bronchial carcinoma.
- Lung collapse.

2] Mediastinal disease:

- Cancer oesophagus: infiltrating the lung.

3] Subdiaphragmatic disease:

- Amoebic liver abscess.
- Subphrenic abscess.

4] Chest wall disease:

- Penetrating wounds.
- Osteomyelitis of: *sternum, ribs or vertebrae.*

B. Extra – thoracic causes:

- Pyaemia: (*pyaemic abscess*)
 - May occur due to infective endocarditis, osteomyelitis.
 - The causative organism is usually: *Staph. aureus.*

PATHOLOGY

1. Primary (inhalation) lung abscess:

A. Site:

- Solitary.
- More common in the right lower lobe because the right bronchus is wider, and in direct continuity with the trachea.

B. Stage:

1) Pneumonic stage:

- There is an area of consolidation (pneumonic patch), and if it is superficial, the covering pleura will show acute pleurisy.

2) Stage of acute abscess:

- Tissue necrosis occurs in the consolidated area producing a cavity with a necrotic wall.
- The covering pleura shows acute pleurisy.

3) Stage of chronic abscess:

- The wall of the cavity becomes thickened by fibrosis.
- The covering pleura may show fibrous adhesions.

2. Pyaemic abscesses:

- They are usually: *bilateral, multiple, small & of equal sizes.*

CLINICAL PICTURE

1. **Pneumonic stage:** *same as in lobar pneumonia*

2. **Stage of acute abscess:**

Symptoms

- After 1 – 2 weeks, the patient suffers from an attack of severe cough followed by expectoration of: excessive purulent foetid sputum.
- The general condition improves & the temperature drops.
- The case continues as a: SUPPURATIVE SYNDROME:
Paroxysmal cough with expectoration of: excessive purulent foetid sputum related to posture when the patient lies on the healthy side.
- Haemoptysis may occur.

Signs

- **General signs:** Fever, tachycardia & sweating.
- **Chest signs:** Features of a cavity & may be pleurisy.

Inspection

- Shape: normal shape of the chest.
- Movements: limited on the affected side.

Palpation

- Trachea & mediastinum: central.
- TVF: increased.

Percussion

- Dullness: on the affected area, due to cavitation.
- Tenderness: on the affected area, due to pleurisy.

Auscultation

- Breath sound: bronchial breathing.

- Additional sounds: crepitations:

Medium sized
Coarse

- Pleural rub: is usually present.

3. Stage of chronic abscess: (Duration > 2 months)

Symptoms

- Symptoms of: SUPPURATIVE SYNDROME.
- Attacks of: RETENTION SYNDROME:
 - o The draining bronchus becomes obstructed with thick secretions.
 - o So fever rises and sputum diminishes.
 - o After few days the patient coughs repeatedly and expectorates the obstructing plug and symptoms of suppurative syndrome reappear.
- Progressive DETERIORATION OF GENERAL HEALTH.

Signs

General signs:

- o Recurrent fever.
- o Pallor, toxic face, loss of weight.
- o Puffiness of eye lids: due to chronic cough.
- o Clubbing of fingers: due to chronic toxemia.

Chest signs: (Signs of cavity & may be fibrosis)

Inspection

- Shape: Normal, but may be retraction due to ++ fibrosis.
- Movements: Limitation of movements on the affected side.

Palpation

- Trachea & mediastinum: Central, but may be shifted to the same side due to ++ fibrosis.
- TVF: Increased.

Percussion

- Dullness: on the affected area, due to cavitation.

Auscultation

- Breath sound: bronchial breathing.
- Additional sounds: crepitations:

Medium sized
Coarse

COMPLICATIONS

A. General complications

- Toxemia: may lead to *amyloidosis*.
- Bacteremia: metastatic abscesses (e.g. brain).
- Anemia.

B. Chest complications

- Lung:
 - Pneumonia (spread of infection to other parts of the lung).
 - Fibrosis & bronchiectasis around the abscess cavity.
- PLEURA: *Pleurisy, Pleural effusion, Empyema.*

INVESTIGATIONS

I. IMAGING:

1) CXR:

- Cavity with a fluid level.
- May show the cause: *in secondary lung abscess.*
- May show complications.

2) CT chest:

- For accurate diagnosis & localization.

II. LABORATORY INVESTIGATIONS:

1) Sputum examination (C&S):

- To detect the causative organism.

2) Blood picture:

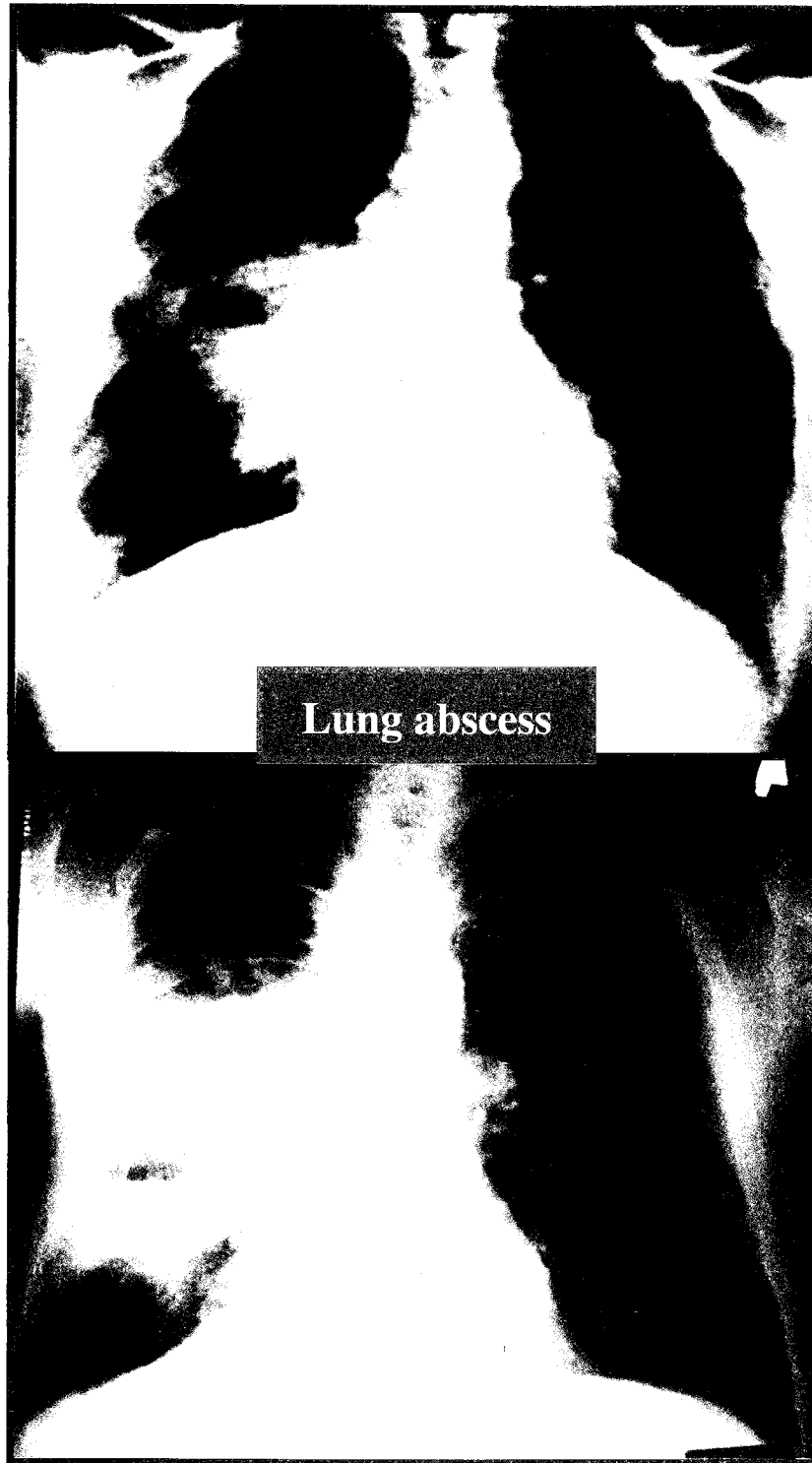
- Leukocytosis: *with shift to the left.*

3) INVESTIGATIONS FOR COMPLICATIONS:

- Culture of aspirated pleural fluid.

III. BRONCHOSCOPY: *indicated to:*

- Localize the site of the abscess
- Exclude the presence of underlying malignancy.
- Detect & remove foreign body.
- Drain pus & inject antibiotics into the cavity.



DIFFERENTIAL DIAGNOSIS

A. Causes of SLS: which is defined as:

"Cough with expectoration of excessive purulent foetid sputum, usually related to posture"

1. Lung abscess:

- Site: localized.
- Onset: acute.
- Periodicity: *absent.*
- Posture: expectoration increases on lying on the healthy side.
- CXR: cavity with a fluid level.

2. Bronchiectasis:

- Site: bilateral & basal.
- Onset: gradual.
- Periodicity: *more in winter , more in the morning.*
- Posture: expectoration increases on leaning forwards.
- CXR: honey-combing.

3. Infected cystic lung:

- Signs of SLS since birth or in early childhood.
- Associated liver & pancreatic affection.
- CXR: soap-bubble appearance.

4. Empyema with broncho – pleural fistula:

- Signs of pyopneumothorax, with:
 - Shifting dullness
 - Positive Methylene blue test.

B. Tuberculous cavity.

TREATMENT

1. Drainage of pus:

- 1) Physical therapy & Postural drainage.
- 2) Bronchoscopic aspiration & injection of antibiotics may be used.

2. Control of infection:

- Antibiotics according to sputum C & S.
- The most commonly used antibiotics are:
 - For anaerobes: Clindamycin or Metronidazole.
 - For Gm +ve, Staph. aureus: Cloxacillin or Vancomycin.
 - For Gm +ve, St. pneumoniae: Penicillin G or Erythromycin.
 - For Gm – ve, Klebsiella: Aminoglycosides or Cephalosporins.
 - For Gm – ve H. influenzae: Ampicillin.

3. Symptomatic Treatment:

- Analgesics & Antipyretics.
- For productive cough:
 - *Mucolytics:* e.g. Bromhexine.
 - *Expectorants:* e.g. Potassium iodide.

4. TREATMENT OF COMPLICATIONS:

- e.g. ttt of pleural effusion.

5. Surgery (segmentectomy or lobectomy) in:

- Chronic or huge abscess not responding to medical treatment.
- Severe recurrent hemoptysis.
- Presence of underlying malignancy
- Complicating empyema or severe bronchiectasis.

BRONCHIECTASIS

DEFINITION

- Abnormal & permanent dilatation of the bronchi.

PATHOLOGY

“2”

I. Lower parts:

- SITE:
 - o Bilateral & Basal.
- BRONCHI:
 - o Are: inflamed & dilated
 - o Full of: mucus & pus.
- SURROUNDING LUNG TISSUE:
 - o May show: consolidation & fibrosis.

II. Upper parts:

- Bilateral emphysema of the upper parts of the lungs occur due to chronic bronchitis resulting from aspiration of infected sputum into the healthy bronchi.

ETIOLOGY

“2”

1. Congenital bronchiectasis:

- Isolated.
- Part of a syndrome:
 - Immotile cilia syndrome:
 - Bronchiectasis.
 - Sinusitis.
 - Male sterility.
 - Kartagener's syndrome:
 - Bronchiectasis.
 - Sinusitis.
 - Dextrocardia.

2. Acquired bronchiectasis:

A. Infection & Fibrosis:

- Recurrent infections lead to destruction & weakening of the musculo-elastic tissue in the wall of the bronchi resulting in their dilatation.
- In addition, peribronchial fibrosis pull on the bronchi from outside leading to further dilatation.
- The **most common** infections causing bronchiectasis are:
 - Viruses: *Adenovirus*.
 - Bacteria: *Staph.aureus, Klebsiella, Anaerobes, H. influenzae, Strept. pneumoniae*.
 - Mycobacteria: *TB*.

B. Bronchial obstruction: which may be either,

a) Partial:

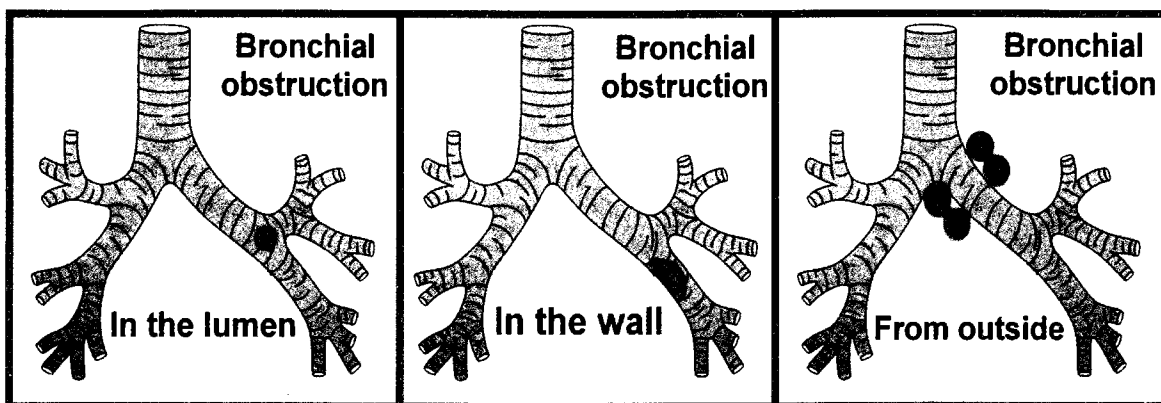
- It acts as a valve mechanism allowing air to enter during inspiration, but preventing it to escape during expiration, so the intra-bronchial pressure will rise progressively leading to bronchiectasis.

b) Complete:

- Collapse resulting from bronchial obstruction increases the negativity of the intrapleural pressure which exerts traction on the bronchi resulting in their dilatation.

- Causes of bronchial obstruction:

- In the lumen: *FB or thick secretions.*
- In the wall: *Tumour.*
- Pressure from outside: *Tumour, LN.*



CLINICAL PICTURE

Symptoms

A. Cough & expectoration: (Suppurative lung syndrome)

- Persistent recurrent cough with expectoration of sputum which is:
 - Excessive.
 - Mucopurulent.
 - Foetid.
 - Increases in the morning & on leaning forwards.
- Onset is gradual & the course is progressive over years with characteristic winter exacerbations.

B. Hemoptysis:

- It may be blood-tinged or frank.
- It may be the only presenting symptom “*bronchiectasis sicca hemorrhagica*”, esp. in cases secondary to TB.

C. Chest Pain: due to:

- Muscular pain because of severe cough.
- Pleuritic pain with occurrence of pleurisy.

D. Dyspnea: due to:

- Fibrosis.
- Obstruction.

E. Wheezing:

- Reflects extensive bronchiectasis.

Signs

1. General signs:

- Recurrent fever.
- Pallor, toxic face, loss of weight.
- Puffiness of eye lids: due to chronic cough.
- Clubbing of fingers: due to chronic toxemia.
- OEDEMA OF LLs: due to,
 - Cor pulmonale & RVF.
 - Renal amyloidosis.
 - Excessive loss of proteins in the sputum.

2. Chest signs:

- In the **basal parts:** signs of consolidation & may be fibrosis.
- In the **upper parts:** signs of chronic bronchitis & emphysema.

Inspection

- Shape:

Basal parts: may be retraction due to ++ fibrosis.

Upper parts: Hyperinflated.

- Movements:

Limitation of movements, mainly in the basal parts.

Palpation

- Trachea & mediastinum:

Central.

- TVF:

Basal parts: ↑.

Upper parts: ↓.

Percussion

- Basal parts: Patchy dullness.
- Upper parts: May be hyper-resonance.

Auscultation

- Basal parts:

- Breath sound: areas of bronchial breathing.

- Additional sounds: crepitations:

Medium sized
Coarse

- Upper parts:

- Breath sound: Vesicular breathing with prolonged expiration.

- Additional sounds: Rhonchi.

COMPLICATIONS

A. General complications

- Toxemia: may lead to *amyloidosis*.
- Bacteremia: metastatic abscesses (e.g. brain).
- Anemia.

B. Chest complications

- Lung:
 - Pneumonia (spread of infection to other parts of the lung).
 - Lung abscess (spread of infection to other parts of the lung).
- PLEURA: *Pleurisy, Pleural effusion, Empyema*.
- Pulmonary hypertension: → cor pulmonale & RVF.
- Respiratory failure: due to associated emphysema.

INVESTIGATIONS

I. IMAGING:

1) CXR:

1. Basal parts:
 - Prominent cystic spaces having the characteristic: "Honey-comb appearance".
 - Opacities around the cysts due to consolidation.
2. Upper parts: "Hypertranslucency" due to emphysema.

2) CT chest: (the most important investigation)

- It provides excellent visualization of the bronchiectatic airways.
- It localizes the site & extent of bronchiectasis before surgery.

3) Bronchography:

- It provides excellent visualization of the bronchiectatic airways.
- It shows the dilated bronchi as: cylindrical, saccular or fusiform.

II. LABORATORY INVESTIGATIONS:

1) Sputum examination (C&S):

- To detect the causative organism.

2) Blood picture:

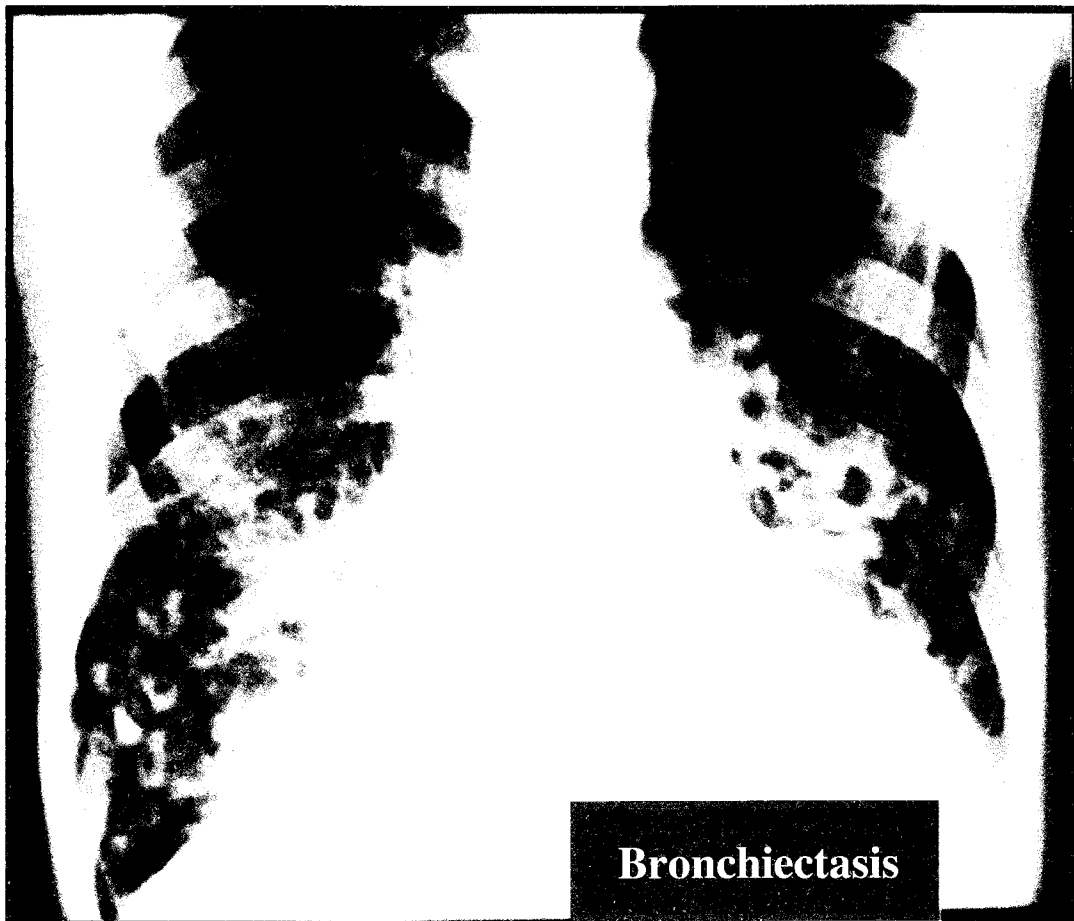
- Leukocytosis: *with shift to the left.*

3) INVESTIGATIONS FOR COMPLICATIONS:

- Culture of aspirated pleural fluid.

III. BRONCHOSCOPY: *indicated to:*

- May reveal the cause in localized bronchiectasis.
- May be used for drainage of pus & injection of antibiotics.



Bilateral & basal:

- Prominent cystic spaces (Honey – comb appearance)
- Opacities around the cysts due to consolidation

DIFFERENTIAL DIAGNOSIS

- Causes of suppurative lung syndrome.
- Causes of hemoptysis.

TREATMENT

1. Drainage of pus:

- 1) Physical therapy & Postural drainage.
- 2) Bronchoscopic aspiration & injection of antibiotics may be used.

2. Control of infection:

- Antibiotics according to sputum C & S.
- The most commonly used antibiotics are:
 - ☒ For anaerobes: Clindamycin or Metronidazole.
 - ☒ For Gm +ve, Staph. Aureus: Cloxacillin or Vancomycin.
 - ☒ For Gm – ve, Klebsiella: Aminoglycosides or Cephalosporins.
 - ☒ For H. influenzae: Ampicillin.
 - ☒ For Strept. pneumoniae: Crystalline penicillin G.

3. Symptomatic Treatment:

- Analgesics & Antipyretics.
- For productive cough:
 - *Mucolytics:* e.g. Bromhexine.
 - *Expectorants:* e.g. Potassium iodide.
- For airway obstruction:
 - *Bronchodilators.*

4. TREATMENT OF COMPLICATIONS:

- e.g. ttt of pleural effusion.

5. Surgery (local resection or lobectomy) in:

- Persistent or recurrent infection not responding to medical treatment.
- Severe recurrent hemoptysis.
- Localised bronchiectasis.

CYSTIC FIBROSIS

(Mucoviscidosis)

DEFINITION

- A hereditary disease (autosomal recessive), affecting mucus-secreting exocrine glands and sweat glands.
- Most of the clinical features are secondary to obstruction by viscid mucus.

CLINICAL PICTURE

1) Chest (Polycystic lung):

- Recurrent infections & SLS, usually in a young age.

2) GIT & Liver:

- Intestinal obstruction in the newly born (meconium ileus).
- Pancreatic insufficiency & malabsorption, secondary diabetes (fibrocystic pancreas).
- Jaundice & later cirrhosis (cystic liver).

3) Genitourinary:

- Male sterility (obliteration of the vas deferens).

INVESTIGATIONS

1) CXR:

- Soap-bubble appearance.
- Multiple fluid levels in cases of infection.

2) Pancreatic function tests:

- May be impaired.

3) Sodium in Sweat:

- Is markedly elevated.

TREATMENT

1- For polycystic lung: same as bronchiectasis.

2- For meconium ileus:

- Enemas & nasogastric suction.
- Surgery is rarely needed.

3- For pancreatic insufficiency:

- Pancreatic enzyme replacement.

RESPIRATORY FUNCTIONS

1. Ventilation.
2. Perfusion.
3. Diffusion.

VENTILATION

DEFINITION

- It is the process of: movement of air in & out of the lungs.
- It is the process of: exchange of air between the lungs and the atmosphere.
- It includes: INSPIRATION & EXPIRATION.

PHYSIOLOGY

INSPIRATION (breathing in): is an ACTIVE process.

- It occurs when the muscles of the diaphragm and chest wall contract.
- The contraction of these muscles will:
 1. Expand the chest wall, the pleura, the lung & therefore will allow air to enter.
 2. Lowers the pressure inside the chest, & thus lowers the pressure in the airways:
 - Pressure gradient occurs from mouth to alveoli, so air rushes in.

EXPIRATION (breathing out): is a PASSIVE process.

- As the muscles relax, the elastic recoil of the lungs puts pressure on the gases inside.
- The pressure in the chest is now higher than the outside pressure:
 - Pressure gradient occurs from alveoli to mouth, so air rushes out.

- Ventilation will depend on:

1. Diameter of the airways.
2. Compliance of: chest wall, pleura, lungs.
3. Neuromuscular apparatus.

Neuromuscular apparatus

I. RESPIRATORY CENTRE in the *medulla*; is controlled by:

A) Feedback from afferent receptors:

Sensors

A B C

1. **AIRWAY RECEPTORS** (Slowly adapting stretch receptors)
 - Location: walls of the bronchi.
 - Sensed by: expansion of the airways at the end of inspiration.
 - Function: send inhibitory impulses to **RC** through the vagus to terminate inspiration (*Protective Hering-Breuer reflex*).
2. **BARORECEPTORS** (Pressure receptors)
 - Location: carotid sinus.
 - Sensed by: changes in the arterial BP.
 - Function: modulate ventilation according to those changes.
3. **CHEMORECEPTORS**
 - Location: medulla (central), carotid arteries, aa (peripheral).
 - Sensed by: changes in PCO₂ (central), PO₂ (peripheral), pH.
 - Function: modulate ventilation according to those changes.
4. **OTHER RECEPTORS** (Proprioceptors)
 - Location: muscles, tendons, joints.
 - Sensed by: movement during exercise.
 - Function: send stimulatory impulses to **RC**.

B) Cerebral cortex:

- Provides some voluntary control of breathing.

II. NEURAL PATHWAY:

Conductors

- AHCs (Cervical & Thoracic segments of the spinal cord).
- Respiratory nerves (Phrenic & Intercostals nerves).
- NMJ.

III. RESPIRATORY MUSCLES.

Effectors

HYPOVENTILATION

ETIOLOGY

1. Obstructive hypoventilation: (↓ diameter of airways)

- a. Upper respiratory tract obstruction: **e.g.**
 - Inhaled FB, laryngeal spasm, laryngeal oedema.
- b. Lower respiratory tract obstruction: **e.g.**
 - Bronchial asthma.
 - COPD.

2. Restrictive hypoventilation:

- a. Decreased compliance of:
 - Lungs: ILD.
 - Pleura: Massive effusion , Tension pneumothorax.
 - Chest wall: Chest deformities, scleroderma, marked obesity (*Pick synd*).
- b. Disorders of neuromuscular apparatus:
 - CNS: Head injury, CVS, Drugs (*opiates & barbiturates*).
 - AHCs: MND, Poliomyelitis.
 - PN: Polyneuropathy, **e.g.** GBS.
 - NMJ: Myasthenia gravis.
 - Muscle: Myopathies.

MANIFESTATIONS

- Hypoxia.
- Hypercapnia.

DIFFUSION

DEFINITION

- It is the process of gas exchange between the alveolar air & the pulmonary capillary blood.
- It occurs through the alveolo – capillary membrane.

PHYSIOLOGY

- Diffusion will depend on:

1. Ventilation – perfusion matching:

- *Normally*, gas exchange depends on the proper matching of ventilation and perfusion, **i.e.** there should be equal distribution of the inspired air and the perfusing blood in different parts of the lungs (V / Q ratio).
- *Abnormally*, gas exchange will become impaired if there is V / Q mismatch.

Causes of Ventilation – perfusion mismatch

- Increased V / Q ratio: (**dead space effect**)
 - It means ventilation of unperfused areas of the lungs, e.g. *pulmonary embolism*.
- Decreased V / Q ratio: (**shunt effect**)
 - It means perfusion of unventilated areas of the lungs, e.g. *pneumonia*.

2. Surface area of diffusion.

3. Intact alveolo-capillary membrane.

4. Pressures of O₂ in the alveolar air & CO₂ in the capillary blood.

IMPAIRED DIFFUSION

ETIOLOGY

- ILD.
- Emphysema.
- Pulmonary oedema.
- Pulmonary embolism.
- Pneumonia.

MANIFESTATIONS

- Hypoxia.
- Normocapnia.

PERFUSION

- It is the process by which the pulmonary circulation delivers blood to the gas exchange units so that: O₂ uptake & CO₂ elimination can occur.

Respiratory Function Tests

I. Tests for specific pulmonary functions:

A. VENTILATION TESTS:

1. Respiratory volumes & capacities: (using the spirometer)
 - See later.
2. Expiratory flow rates:
 - Forced expiratory volume in the first second (**FEV₁**):
 - Normally: ~ 3800 ml.
 - Normally: $FEV_1 / FVC \sim 80\%$ (Timed vital capacity).
 - Peak expiratory flow rate (**PEFR**).

These tests are impaired in: **OBSTRUCTIVE HYPOVENTILATION**

3. Lung compliance:

- The ratio of change in volume of the lung to change in intrapleural pressure.

4. Ventilation scan:

- Using radioactive Xenon (see pulmonary embolism).

B. DIFFUSION TESTS:

- Diffusing capacity: (CO transfer factor)
 - It measures the quantity of CO that will diffuse in a time unit from the alveolar gas into the capillary blood.
 - It is a useful measure for the integrity of the alveolo – capillary membrane.

C. PERFUSION TESTS:

1. Pulmonary vascular pressures.
2. Perfusion lung scan: using radioactive albumin (see pulmonary embolism).

II. Tests for general pulmonary functions:

- ABG: PO_2 & PCO_2 .
- Pulse Oximetry.

Tidal Volume:**TV**

- o It is the volume of air inspired & expired during: normal quiet breathing.
- o Normally ~ 500 ml.
- o Resting minute volume (RMV) = TV x RR (16 / min.) = 8000 ml / min.

Residual Volume:**RV**

- o It is the volume of air remaining in the lung: after maximum expiration.
- o Normally ~ 1200 ml.
- o *It increases in:* **COPD**.

Forced Vital capacity:**FVC**

- o It is the volume of air that is maximally expired: after maximum inspiration.
- o Normally ~ 4800 ml (ERV + IC)
- o *It decreases in:* *all cases of hypoventilation, especially restrictive hypoventilation.*

Total Lung Capacity:**TLC**

- o It is the volume of air that the lungs contain when they are fully expanded.
 - o Normally ~ 6000 ml (RV + FVC)
 - o *It decreases in:* *restrictive hypoventilation.*
-

Expiratory Reserve Volume:**ERV**

- o It is the additional volume of air that can be exhaled after a normal tidal breath out.
- o Normally ~ 1200 ml.

Inspiratory Reserve Volume:**IRV**

- o It is the additional volume of air that can be inhaled after a normal tidal breath in.
- o Normally ~ 3100 ml.

Functional Residual Capacity:**FRC**

- o It is the volume of air left in the lungs after a normal tidal breath out.
- o Normally ~ 2400 ml (RV + ERV)

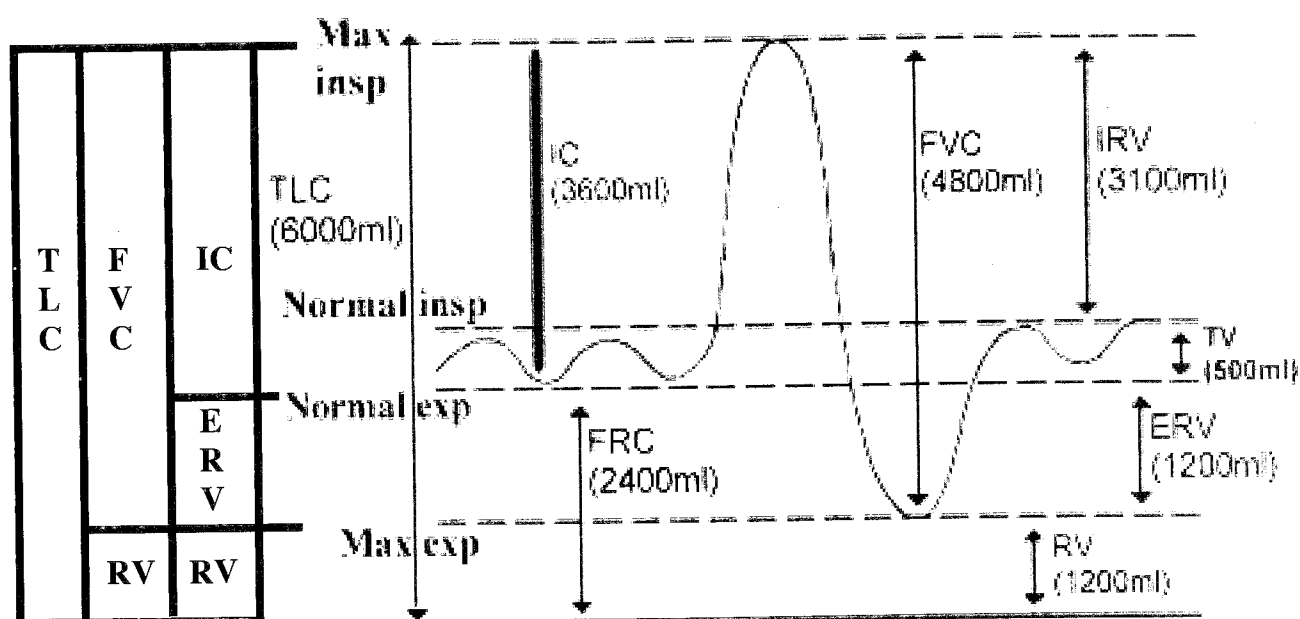
Inspiratory Capacity:**IC**

- o It is the maximum volume of air that can be inhaled after a normal tidal breath out.
 - o Normally ~ 3600 ml (TV + IRV)
-

Maximum Breathing Capacity:**MBC**

- o The maximum volume of air that can be respired in one min. by the deepest & fastest breathing.
- o Normally, 120 L / min.

RESPIRATORY VOLUMES

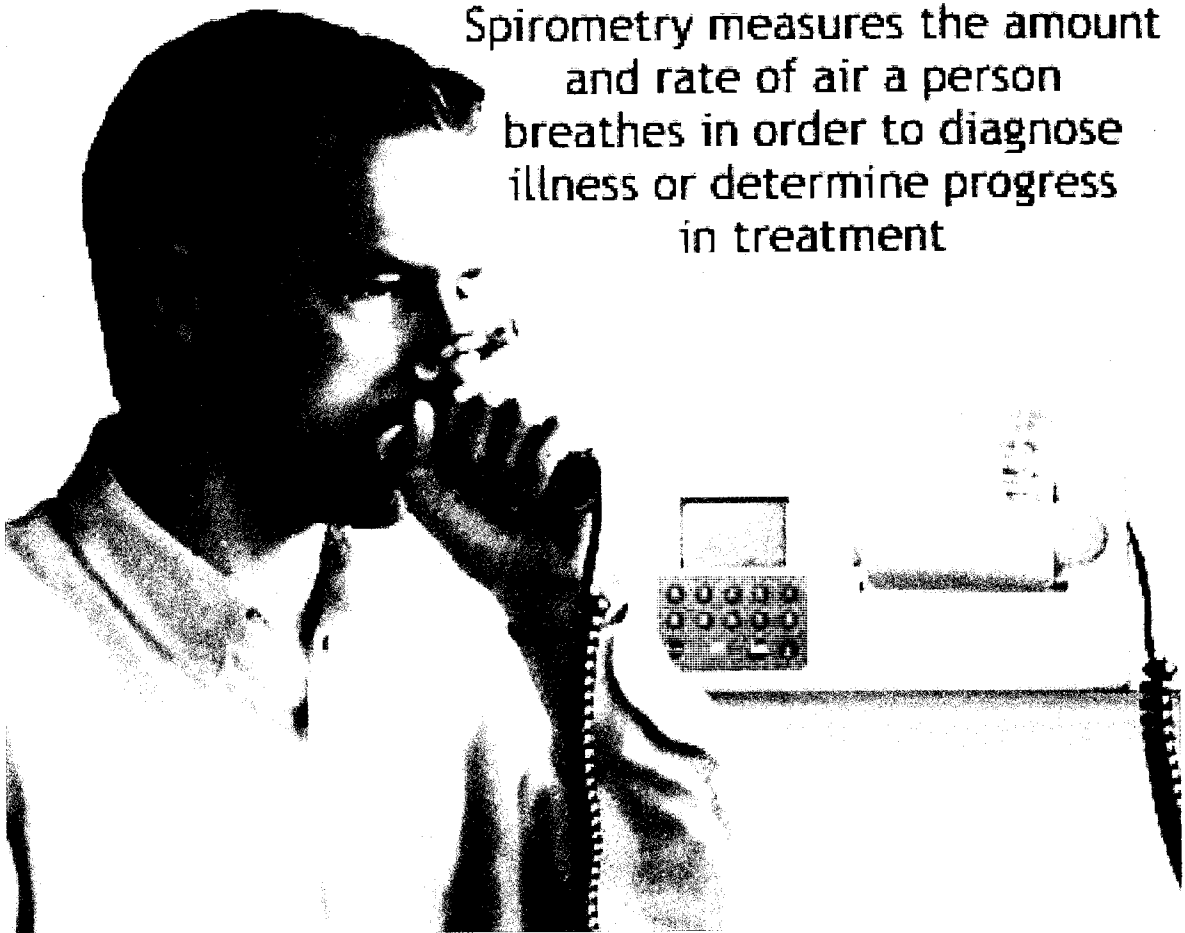


Lung Volumes measured with a spirometer during quiet breathing with one maximum breath. Values shown are for an average-sized healthy young male.

<i>RV</i>	<i>Residual volume</i>	<i>FRC</i>	<i>Functional residual capacity</i>
<i>ERV</i>	<i>Expiratory reserve volume</i>	<i>TV</i>	<i>Tidal volume</i>
<i>IRV</i>	<i>Inspiratory reserve volume</i>	<i>FVC</i>	<i>Forced vital capacity</i>
<i>TLC</i>	<i>Total lung capacity</i>	<i>IC</i>	<i>Inspiratory capacity</i>

SPIROMETER

Spirometry measures the amount and rate of air a person breathes in order to diagnose illness or determine progress in treatment



Pattern of restrictive hypoventilation in RFTs

- Respiratory volumes & capacities:
 - Decreased: FVC.
 - Normal: RV.
 - Decreased: TLC.
- Expiratory flow rates:
 - Normal: FEV₁ / FVC.
- Decreased lung compliance.

Pattern of obstructive hypoventilation in RFTs

- Respiratory volumes & capacities:
 - Decreased: FVC.
 - Increased: RV.
 - Increased: TLC.
- Expiratory flow rates:
 - Decreased: FEV₁ / FVC.
- Increased lung compliance.

RESPIRATORY FAILURE

DEFINITION

- Laboratory diagnosis characterized by:

- HYPOXIA (< 60 mm Hg) with or without:
- HYPERCAPNEA (> 50 mm Hg),

due to a disease affecting respiration.

ETIOLOGY

- 1- Impaired diffusion.
- 2- Hypoventilation.

}

See before

TYPES

A) According to the gas defect:

1. HYPOXEMIC TYPE (TYPE I): “mainly due to ↓ diffusion”
 - HYPOXIA: with normocapnia or hypocapnia.
2. HYPERCAPNIC TYPE (TYPE II): “mainly due to ↓ ventilation”
 - HYPOXIA: with HYPERCAPNIA.

B) According to the clinical onset:

1. ACUTE TYPE:
 - Onset: acute.
 - pH in Type II: markedly ↓↓ (respiratory acidosis).
2. CHRONIC TYPE:
 - Onset: gradual.
 - pH in Type II: slightly ↓↓ (renal compensation).

CLINICAL PICTURE

- 1- Manifestations of: HYPOXIA.
- 2- May be manifestations of: HYPERCAPNEA.
- 3- Manifestations of the cause: **e.g.**
 - Features of COPD: chronic respiratory failure.
 - Features of GBS: acute respiratory failure.

MANIFESTATIONS OF HYPOXIA

1. Acute hypoxia:

- BP: Hypotension.
- PULSE: Tachycardia, Arrhythmias.
- RESPIRATION: Tachypnea, Dyspnea.
- **C**entral **C**yanosis.
- **D**ROWSINESS: convulsions, coma.
- **D**EATH.

2. Chronic hypoxia:

- Headache.
- Polycythemia (secondary).
- **C**or pulmonale (secondary to pulmonary hypertension).
- **C**entral **C**yanosis.
- **C**lubbing.
- Apathy, fatigue, drowsiness.

MANIFESTATIONS OF HYPERCAPNIA

1. Acute hypercapnia:

- **A**sterixis (*flapping tremors*).
- **A**cidosis (*respiratory*).
- PULSE: Tachycardia, Arrhythmias.
- RESPIRATION: Tachypnea, Dyspnea.
- **D**ROWSINESS: convulsions, coma.
- **D**EATH.

2. Chronic hypercapnia:

- **A**sterixis (*flapping tremors*).
- CO₂ narcosis (Hypercapnic encephalopathy): Hypersomnia, drowsiness.
- INCREASED ICT, PAPHILLOEDEMA.

INVESTIGATIONS

1- Tests for specific pulmonary functions.

2- Tests for general pulmonary functions:

- a. ABG: (PO₂ , PCO₂) & (pH , HCO₃).
- b. Pulse Oximetry.

3- Investigations of the cause: **e.g.**

- Investigations of COPD: chronic respiratory failure.
- Investigations of GBS: acute respiratory failure.

TREATMENT

1- Admission to hospital: *in a respiratory ICU.*

2- Supportive treatment:

A) Improvement of ventilation:

1. Maintenance of patent airways.
2. Elimination of retained secretions:
 - Encourage the patient to cough.
 - Respiratory exercises.
 - Expectorants **e.g.** *potassium iodide.*
 - Liquefaction of sputum:
 - Adequate hydration.
 - Mucolytics **e.g.** *bromhexine.*
 - Suction of secretions through:
 - Catheters.
 - Endotracheal tube.

B) Oxygen inhalation.

C) Mechanical ventilation.

3- Treatment of the cause: **e.g.**

- Treatment of COPD: chronic respiratory failure.
- Treatment of GBS: acute respiratory failure.

4- Treatment of complications: **e.g.**

- Treatment of *pulmonary infections.*
- Treatment of acidosis: (in acute Type II RF).

CHRONIC BRONCHITIS

DEFINITION

A condition characterized by excessive mucus secretion from the bronchial tree, in which there is productive cough every day, or most days, for at least 3 months of the year, for at least 2 successive years.

ETIOLOGY & PREDISPOSING FACTORS

(7 S)

1. **S**ex: males more than females.
 2. **S**usceptibility: family history common.
 3. **S**moking: (*the most common cause*). }
 4. **S**mog: atmospheric pollution. }
- Bronchial irritation
-
5. **S**inusitis: chronic sinusitis predisposes to bronchitis.
 6. **S**uperinfection: St. pneumoniae & H. influenza.
 7. **S**ocial class: lower socio economic groups than higher.
 8. OTHERS:
 - a. Chronic lung congestion (*LVF*).
 - b. Chronic lung plethora (*congenital heart disease with Lt to Rt shunt*).
 - c. Bronchiectasis.
 - d. Allergic factors: may play a role.

PATHOLOGY

- There are **3 types** which represent gradual increase in the severity of the disease:

1. Chronic simple bronchitis:

- There is hypertrophy of the mucus-secreting glands.
- The patient expectorates whitish mucoid sputum.

2. Chronic mucopurulent bronchitis:

- There is secondary infection most commonly with:
St. pneum. & H. influenzae.
- The patient expectorates yellowish mucopurulent sputum.

3. Chronic obstructive bronchitis:

- There is chronic irreversible airway obstruction, mainly affecting the small airways, due to:
 - Thickening of the bronchial wall.
 - Peribronchial fibrosis.
- This condition may be complicated by emphysema.

EMPHYSEMA

DEFINITION

- A **pathologic term** indicating enlargement of the air spaces distal to the terminal bronchioles due to dilatation and / or destruction of the alveolar walls.
- When the expansion of the air spaces is due to dilatation only, the condition may be termed “ false emphysema ” & it does not cause respiratory dysfunction.
- When destruction of the alveolar walls is the main pathology, the condition is termed: “ true emphysema.”

ETIOLOGY

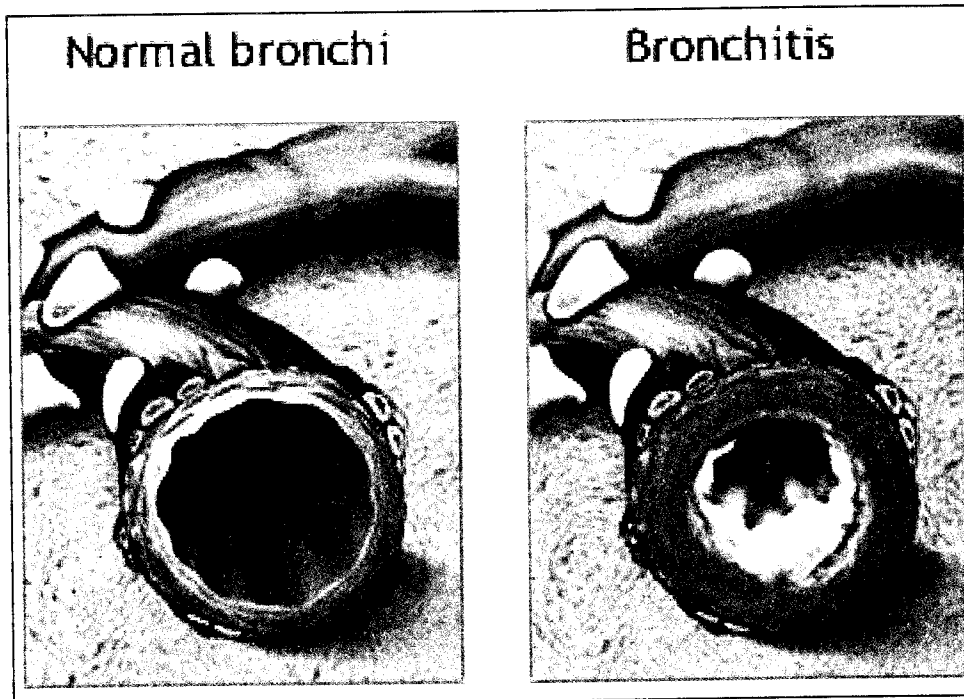
I. False emphysema:

1. **Senile emphysema:** (*atrophic emphysema*)
 - Occurs in old age due to weakness of the alveolar walls.
2. **Compensatory emphysema:**
 - Occurs in lobules adjacent to areas of consolidation, collapse, fibrosis or resection.

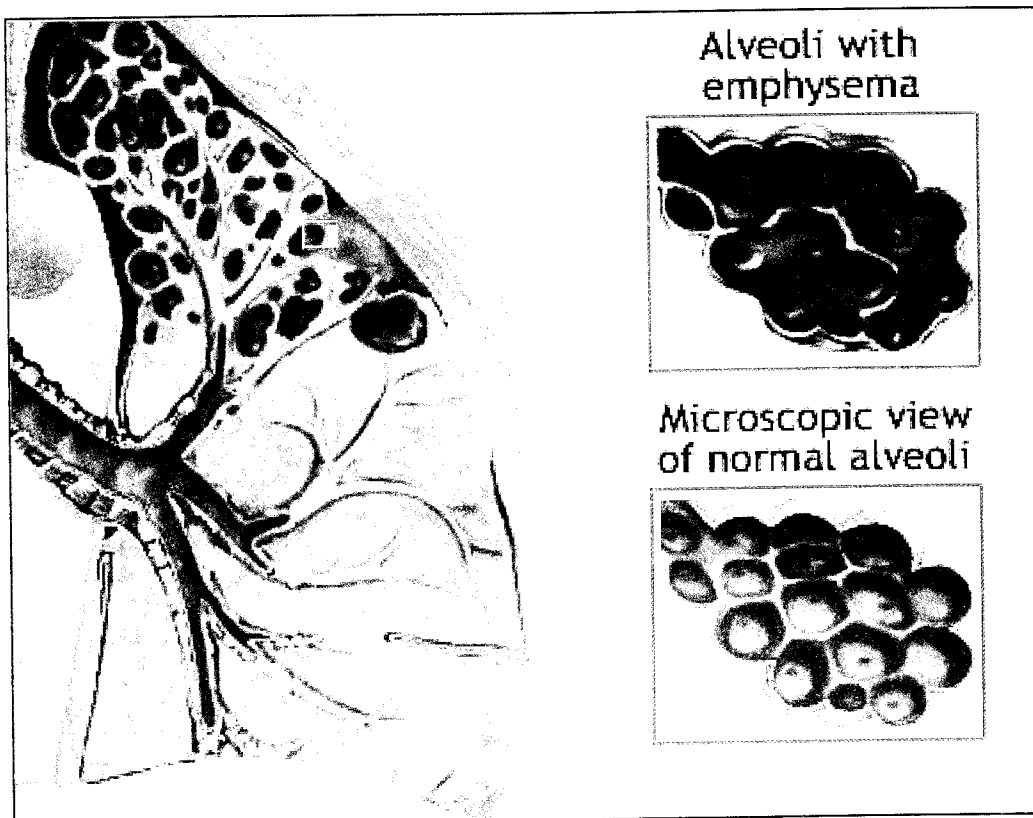
II. True emphysema:

1. **Primary emphysema:**
 - Occurs due to deficiency of serum alpha 1- antitrypsin.
2. **Secondary emphysema:**
 - This is the most important type & occurs as a complication of:
 - Chronic obstructive bronchitis (*the most common cause*).
 - Bronchial asthma.

BRONCHITIS



EMPHYSEMA



EMPHYSEMA versus CHRONIC OBSTRUCTIVE BRONCHITIS

- In emphysema:

- Impaired diffusion due to destruction of the alveolar walls is the major abnormality leading to:

HYPOXIA & NORMOCAPNEA.
- Due to HYPOXIA, stimulation of the respiratory center occurs & results in: severe DYS-PNEA which partially corrects the hypoxia.
- Conclusion:
 - Presence of: severe dyspnea.
 - Absence of: Central cyanosis, PH, corpulmonale, RVF.
 - This type is: “**Pink puffers**”, **Type A**, or **Emphysematous Type**.

- In chronic obstructive bronchitis:

- Impaired ventilation due to airway narrowing is the major abnormality leading to:

HYPOXIA & HYPERCAPNEA.
- Due to UNKNOWN REASON, stimulation of the respiratory center does not occur, this results in: absence of severe DYS-PNEA.
- Conclusion:
 - Absence of: severe dyspnea.
 - Presence of: Central cyanosis, PH, corpulmonale, RVF.
 - This type is: “**Blue Bloaters**”, **Type B**, or **Bronchitic Type**.

	Pink Puffers	Blue Bloaters
- Dyspnea	- Severe	- Very mild
- Sputum	- Small volume	- Large volume
- Central cyanosis	- <u>Absent</u>	- <u>Present</u>
- Pulmonary hypertension	- Very mild or <u>absent</u>	- <u>Present</u>
- Cor pulmonale & RVF	- Very late or <u>absent</u>	- <u>Present</u>
- Chest examination	- Hyperinflation	- Wheezes
CXR	- Hypertranslucency	- No Hypertranslucency
ABG		
- PO ₂	- Mild decrease	- Severe decrease
- PCO ₂	- Normal	- High

HOWEVER: there is usually overlap between both types because they frequently coexist. So, it is difficult to differentiate them into 2 separate clinical types.

Chronic Obstructive Pulmonary Disease

COPD

DEFINITION

- A group of chronic & slowly progressive respiratory disorders characterized by: reduced expiratory flow rates.
- It includes: chronic obstructive bronchitis, & emphysema which usually co-exist.

PATHOPHYSIOLOGY

1. Impaired ventilation:

- This is due to:

“obstructive hypoventilation”

narrowing of the airways.

2. Impaired diffusion:

- Destruction of the alveolar walls causes: diminished surface area of diffusion.

3. Impaired perfusion:

- Destruction of the alveolar septa causes: loss of the capillaries.

4. Hyperinflation:

- It is due to: increased residual volume due to obstruction.
- It leads to: signs of hyperinflated chest.

5. Cardiovascular abnormalities:

I. Pulmonary hypertension: due to:

1. Hypoxia: will cause:

- Direct VC of the pulmonary arteries.
- Increased blood viscosity due to polycythemia.

2. Reduction of the pulmonary vascular bed: due to:

- Loss of the capillaries: due to destruction of the alveolar septa.
- Compression of the capillaries: due to ↑ intra – alveolar pressure.

II. Hypoxic cor pulmonale.

6. Renal & hormonal abnormalities:

- Chronic hypoxia & hypercapnea have been shown to cause increased levels of:
renin, aldosterone, noradrenaline.
- Salt & water retention will occur: even in the absence of RVF.

CLINICAL PICTURE

Type of patient

- Usually a male, chronic heavy smoker, above 50 years.

Symptoms

1. Long history of chronic bronchitis:

- Chronic cough: with expectoration of mucoid sputum.
- Chronic cough: with expectoration of mucopurulent sputum.
- Chronic cough: with gradual progressive dyspnea & wheezing.

2. Chest pain, due to:

- Pain in intercostals muscles.. from chronic cough.
- Pneumothorax..... from rupture of emphysematous bullae.
- Pleurisy from complicating pneumonia.

3. Oedema of lower limbs, due to:

- RVF.
- Salt & water retention.

4. Symptoms of complications, e.g. respiratory failure.

Signs

GENERAL SIGNS

1. Vital signs:

PULSE:

A) Volume:

In early cases:

- Big pulse volume: due to VD effect of hypoxia.

In late cases:

- Small pulse volume: due to PH & RVF.

In severe cases:

- Pulsus paradoxus.

B) Rhythm:

Arrhythmias: especially, MAT, AF.

RESPIRATORY RATE:

Tachypnea: with working accessory respiratory muscles.

2. Head examination:

- Puffiness of the eye lids: due to chronic cough.
- Central cyanosis: may be present.

3. Neck examination: “Congested pulsating”

- Increased intrathoracic pressure.
- RVF.

4. Upper limbs:

- Mild clubbing: *is the rule.*
- Marked clubbing: *occurs if there is associated bronchiectasis.*

5. Lower limbs: “Oedema”

- RVF.
- Salt & water retention.

6. Abdomen:

1. Liver:

- The lower border of the liver may be palpable due to:
 - a) *Ptosed liver:* due to hyperinflation (**non tender**).
 - b) *Enlarged liver:* due to RVF (**tender**).

2. Ascites:

- It is due to RVF.

7. General signs of complications, e.g. respiratory failure, *especially:*

- **C**entral **C**yanosis.
- **A**sterixis (*flapping tremors*).
- CO₂ narcosis (Hypercapnic encephalopathy): Hypersomnia, drowsiness.

CHEST SIGNS

Inspection

- Shape: barrel shaped chest.
- Movement: decreased bilaterally.

Palpation

- Trachea: central.
- TVF: decreased bilaterally all over the chest.

Percussion

- Hyperresonance: all over the chest.
- Encroachment on: the normal hepatic & cardiac dullness.

Auscultation

- Breath sounds: vesicular with prolonged expiration.
- Additional sounds: generalized rhonchi, mainly expiratory, may be early inspiratory crepitations.

COMPLICATIONS

- | | | |
|---|---|------------------------------|
| 1. Respiratory failure. | } | <u>Failure</u> |
| 2. Right sided heart failure following cor pulmonale. | | |
| 3. Left sided heart failure. | | |
| 4. Pulmonary infections. | } | <u>Chest complications</u> |
| 5. Pneumothorax. | | |
| 6. Bronchiectasis. | | |
| 7. Polycythemia. | } | <u>General complications</u> |
| 8. Salt & water retention. | | |
| 9. Complications of chronic cough. | | |

Causes of Left sided HF in COPD

1. Hypoxia: leading to myocardial ischemia.
2. Acidosis: leading to myocardial depression.
3. Volume overload due to: hyperdynamic circulation due to VD.
4. Increased blood viscosity due to: polycythemia.
5. Reversed Bernheim effect.
6. Associated disease of the left side of the heart, especially CAD.

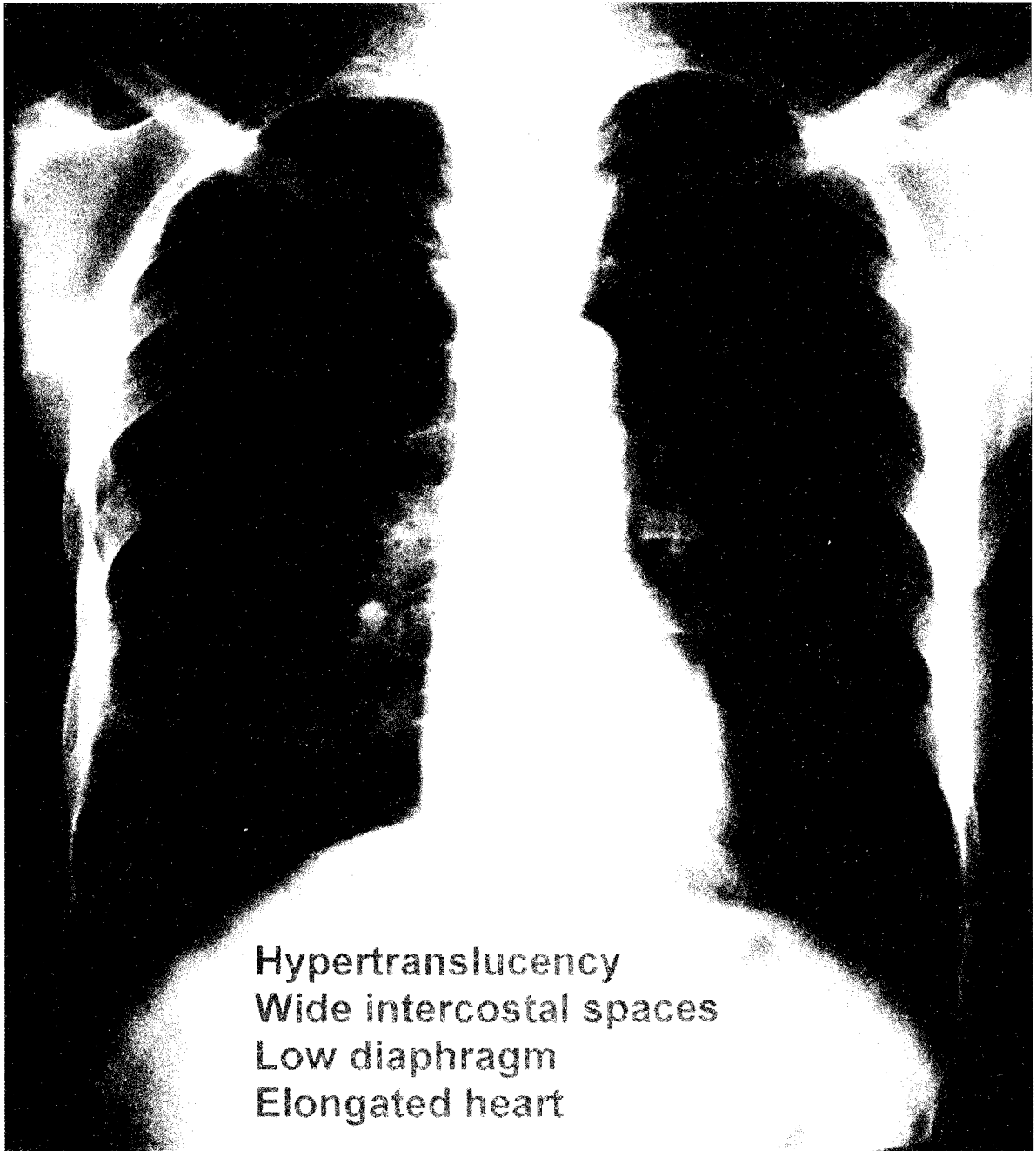
INVESTIGATIONS

1. CXR:

a) Signs of hyperinflation:

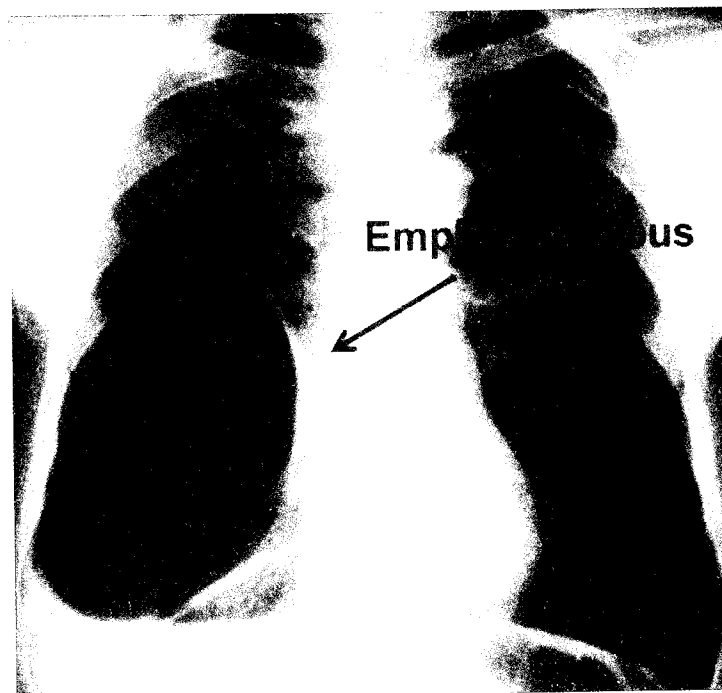
- Hypertranslucency of the lung fields.
- Wide intercostal spaces.
- Low flat diaphragm.
- Heart shadow is elongated “ribbon-shaped heart”.
- May be emphysematous bullae.

b) Increased bronchovascular markings.





Low diaphragm, Elongated heart, ↑ bronchovascular markings



2. ECG:

- Arrhythmias, e.g. (MAT, AF).
- Chamber enlargement, e.g. (RV++ & RA++).
- CAD.
- Low voltage.

3. Respiratory function tests:

Specific pulmonary function tests:

- a) Ventilation tests:
 - Features of obstructive hypoventilation.
- b) Diffusion tests:
 - Disturbed tests of diffusion: decreased CO transfer factor.
- c) Perfusion tests:
 - Disturbed tests of perfusion.

General pulmonary function tests: (ABG)

- Hypoxia.
- Hypercapnea.
- Increased bicarbonate.

4. Blood picture:

- May show: secondary polycythemia.

5. Serum alpha 1-antitrypsin:

- Decreased in primary emphysema.

TREATMENT

1. Avoid further bronchial irritation:

- Stop smoking.
- Avoid atmospheric pollution.

2. Treatment of complications:

- e.g. respiratory infections, antibiotics according to: C & S.
- e.g. respiratory failure.

3. Symptomatic treatment:

- Expectorants, e.g. potassium iodide.
- Mucolytics, e.g. bromhexine.
- Bronchodilators, e.g. β_2 -stimulants.
- Corticosteroids, e.g. prednisone 1 mg / Kg orally daily in:
 - *Patients not responding to bronchodilators.*
- OXYGEN THERAPY.

ASTHMA

DEFINITION

- It is a CLINICAL SYNDROME characterized by **recurrent episodes** of: **airway obstruction** that resolve spontaneously or by treatment.
- The clinical episodes include 3 main symptoms: cough, dyspnea, wheezing.

PATHOLOGY

- It is a common chronic INFLAMMATORY condition of the airways.
- It has 3 main characteristics:
 1. Airflow **limitation**: reversible spontaneously or by treatment.
 2. Airway **hyper-responsiveness**: to a wide range of stimuli.
 3. Airway **INFLAMMATION**: the bronchial wall shows:
 - Epithelial damage.
 - Cells: Eosinophils, Mast cells, T-lymphocytes, Macrophages.
 - ✓ - Goblet cell hyperplasia → ↑ mucus production.
 - ✓ - Oedema.
 - ✓ - Smooth muscle hypertrophy.

} **Bronchial narrowing**

With time, chronic inflammation → *submucosal fibrosis* → persistent airway obstruction

CLASSIFICATION

1. Extrinsic asthma (Allergic asthma):

- There is a definite external cause, especially antigen or allergen.
- It occurs in ATOPIC individuals.

2. Intrinsic asthma (Idiosyncratic):

- There is no definite external cause, no antigen no allergen.
- Non – antigenic stimuli may be responsible.

Patients commonly show features of both types of asthma.

ETIOLOGY & PATHOGENESIS

I. Extrinsic asthma

(atopy is the major factor)

1. It occurs in atopic individuals:

- It runs in families.
- Associated atopic diseases: e.g. allergic rhinitis.
- Early – onset asthma: starts usually in childhood.
- Skin tests: positive.
- Serum IgE level: increased.

2. It occurs due to exposure to allergic stimuli:

- Inhaled allergens, e.g. house dust.
- Ingested allergens, e.g. fish, eggs.
- Injected allergens, e.g. penicillin.
- Contact

3. MECHANISM:

a. Sensitization:

- When allergens are inhaled for the first time, specific **IgE antibodies** are formed and bind to receptors on the surface of **Mast cells** of the tracheo-bronchial tree.

b. Stimulation: (initial response)

- When these allergens are inhaled for the second time & repeatedly, they will bind to IgE antibodies → stimulation of mast cells.
- Mast cells will degenerate → release of **Mediators** → asthma.

c. Signaling: (secondary response = late-onset response)

- Following stimulation of mast cells, these cells begin to signal other cells (lymphocytes, macrophages & epithelial cells) → upregulation of these cells, extension of inflammation & more release of mediators.

d. Migration: of eosinophils into the airways occurs under the effect of chemotactic cytokines.

e. Activation: of eosinophils under the effect of cytokines (IL-5) → release of:

- Toxic products (e.g. Major basic protein).
- Mediators (e.g. Leukotrienes & PAF).

f. Epithelial damage: occurs under the effect of eosinophil products.

II. Intrinsic asthma (airway hyper-responsiveness is the major factor)

1. It is not related to atopy or allergy:

- It does not run in families.
- No associated atopic diseases.
- Late – onset asthma: starts usually in middle age.
- Skin tests: negative.
- Serum IgE level: normal.

2. It occurs due to exposure to non – allergic stimuli (triggers):

- Environmental: e.g. pollution & industrial materials.
- Exposure to: respiratory tract infections (*esp. viruses*).
- Exposure to: cold air.
- Exercise: exercise – induced asthma.
- Emotional stress.
- DRUGS: Aspirin (& other NSAIDs), B-blockers.

3. MECHANISM:

- Probably these patients have highly sensitive Vagal receptors in the tracheo-bronchial tree.
- Non-antigenic stimulation of these receptors results in:
 - o Reflex bronchospasm.
 - o Stimulation: of Mast cells → release of Mediators.
 - o Signaling: as mentioned above.
 - o Migration: as mentioned above.
 - o Activation: as mentioned above.
 - o Epithelial damage: as mentioned above.

Mediators involved in asthma

- Histamine.
- Adenosine.
- Serotonin.
- Prostaglandins.
- Kinins.
- LEUKOTRIENES.
- CYTOKINES.
- PAF (Platelet activating factor).

CLINICAL PICTURE

I. ATTACKS OF ASTHMA:

Symptoms “Attacks”

- **Timing:**
 - o Usually occur in late night & early morning due to **High vagal tone.**
- **Description:**
 - o Typically: a **Triad** of, Dyspnea, cough, wheezing.
 - o Cough-variant asthma: cough (esp. nocturnal) may be the only presenting C/O.
 - o Expectoration: viscid sputum (mucous pellets).
 - o Association: anxiety, sweating.
- **Duration:** (Variable)
 - o Few minutes..... to several hoursor even days.
 - o Resolve spontaneously or by treatment.

Signs

1. During the attack: “ Signs of Hyperinflation & Airway obstruction”

Inspection

- Shape: barrel shaped chest.
- Movement: decreased bilaterally.

Palpation

- **TTrachea:** central.
- **TVF:** decreased bilaterally.

Percussion

- Hyperresonance.

Auscultation

- Breath sounds: vesicular with prolonged expiration.
- Additional sounds: generalized rhonchi, mainly expiratory.

2. In between the attacks:

- The chest is usually free, unless:
 - Bronchial asthma is accompanied with chronic bronchitis.
 - Submucosal fibrosis occurs in chronic cases → persistent obstruction.

II. CLASSIFICATION OF ASTHMA:

Asthma severity is divided into the same classes in the:

NAEPP¹, and **GINA**² guidelines.

Classification is based on:

1. History of asthma symptoms.
2. Lung functions.

}

Without ttt

NAEPP / GINA Classification of Asthma Severity

	Symptoms/Day	Symptoms/Night	PEFR or FEV ₁
<u>STEP 1</u> <i>Mild Intermittent</i>	≤ 2 times a week No symptoms between attacks	≤ 2 times a month	≥ 80%
<u>STEP 2</u> <i>Mild Persistent</i>	> 2 times a week but < 1 time a day Attacks may affect daily activity	> 2 times a month	≥ 80%
<u>STEP 3</u> <i>Moderate Persistent</i>	Daily Attacks affect daily activity	> 1 time a week	60% - 80%
<u>STEP 4</u> <i>Severe Persistent</i>	Continuous Severe limitation of daily activity	Frequent	≤ 60%

- An asthmatic patient belongs to a certain class if:
[**ONLY** one feature of that class is present "without treatment"].

¹ **NAEPP:** The **N**ational **A**sthma **E**ducation and **P**revention **P**rogram

² **GINA:** The **G**lobal **I**nitiative for **A**sthma

III. **STATUS ASTHMATICUS:**

(acute severe asthma)

- It is a medical emergency:
The severest form of asthma that remains unresponsive to the standard treatment of asthma for several hours.
- It is of variable severity:
It may be either: *severe* or *life – threatening*.

Manifestations of severe asthma:

- RESPIRATION:
 - Inability to complete a sentence in one breath.
 - Tachypnea: RR > 25 breaths per minute.
- PULSE:
 - Pulsus paradoxus.
 - Tachycardia: HR > 110 beats per minute.
- RESPIRATORY FUNCTIONS:
 - Marked decrease of: PEFR & FEV₁ (< 50% of normal).

Manifestations of life threatening asthma:

- Silent chest.
- Central cyanosis.
- Confusion or coma.
- RESPIRATORY FUNCTIONS:
 - Marked decrease of: PEFR & FEV₁ (< 30% of normal).
- ARTERIAL BLOOD GASES (ABG):
 - Marked hypoxemia: PO₂ < 60 mmHg (despite ttt with O₂).
 - Marked hypercapnea: PCO₂ > 45 mmHg.
 - Low or falling pH.

COMPLICATIONS

1. STATUS ASTHMATICUS.
2. COPD.
3. Respiratory failure.
4. Right sided heart failure & cor pulmonale.
5. Complications of: severe cough.
6. Complications of: therapy e.g. corticosteroids.
7. Pneumothorax & pneumomediastinum.
8. Allergic bronchopulmonary aspergillosis (ABPA).

INVESTIGATIONS

1. Pulmonary function tests:

I. VENTILATION: Obstructive hypoventilation (Reversible):

- Decreased PEF & FEV₁ which improve at least 15 % after inhalation of a bronchodilator (i.e. reversible airway obstruction).
- Absent response to inhaled bronchodilators occurs in:
 - a) Asthma in remission (inbetween the attacks).
 - b) Severe longstanding chronic asthma (persistent irreversible obstruction).

II. DIFFUSION:

- CO transfer factor: normal in asthma.

III. Arterial blood gases (ABG):

- PO₂: Decreased.
- PCO₂: Increased.

2. Bronchial provocation tests:

- These tests use Histamine or metacholine (inhaled) to demonstrate: airway hyper-responsiveness especially when cough is the presenting symptom.
- These tests are contraindicated in severe cases with poor lung function.

3. Exercise tests:

- These tests use Treadmill to diagnose: Exercise – induced asthma.

4. CXR: “ little role ”

- Little role in diagnosing asthma: because it is normal in between the attacks.
- During the attack: it may show signs of hyperinflation.
- May show complications: such as pneumothorax, or ABPA.

5. CBC:

- Excessive eosinophils (more marked in case of ABPA).

6. Sputum examination:

- Excessive eosinophils.
- Curschman's spirals.
- Charcot – Leyden crystals.
- Creola bodies.

7. Skin tests:

- To identify the allergen in extrinsic asthma.

8. Serum IgE:

- Increased in most cases of extrinsic asthma.

DIFFERENTIAL DIAGNOSIS

1. From other causes of paroxysmal dyspnea with wheezing:
 - Cardiac asthma.
 - Uremic asthma.
 - Carcinoid syndrome.
 - Pulmonary vasculitis.
2. From other causes of paroxysmal dyspnea:
 - Cardiac dyspnea.
 - Extrinsic allergic alveolitis.
 - Tetany (laryngismus stridulus).
 - Myasthenic crisis.
 - Recurrent pulmonary emboli.
3. From chronic bronchitis.
4. Differentiate between: *extrinsic & intrinsic asthma.*

TREATMENT

1 GENERAL MEASURES

- Avoid exposure to stimuli: whether allergic or non –allergic.
- Treatment of: CHEST INFECTIONS.
- PSYCHOTHERAPY.
- IMMUNOTHERAPY: (HYPOSENSITIZATION)
 - Repeated injection of extracts of the allergen in gradually increasing doses may be beneficial..... why ??
 - It results in production of IgG antibodies which will prevent binding of the allergen to IgE (blocking antibodies).

2 SPECIFIC MEASURES (DRUGS)

1. BRONCHODILATORS

A) Sympathomimetics:

1. Selective β_2 -Agonists: [INHALED]

*THEY HAVE A RAPID ONSET OF ACTION & FEW SIDE EFFECTS.
THEY COULD BE GIVEN PARENTRALLY IN STATUS ASTHMATICUS.*

- Salbutamol: (puff = 100 μ g, 2 puffs tds).
- Terbutaline: (puff = 250 μ g, 2 puffs tds).
- Salmeterol: (puff = 50 μ g, 1 puff bid) LONG ACTING.

2. Non Selective β_2 - Agonists:

THEY ARE OF LITTLE USE BECAUSE OF THEIR SIDE EFFECTS.

- Adrenaline: 0.5 c.c. 1 / 1000 solution SC.
- Isoprenaline: 10 mg SL or by inhalation.
- Ephedrine: 30 mg orally.

B) Xanthines: (Theophylline or Aminophylline)

- Short acting: slow IV infusion in status asthmaticus.
- long acting: orally for long – term control.

2. RECEPTOR ANTAGONISTS

A) Anticholinergic bronchodilators: “ Acetylcholine antagonists ”

- Ipratropium bromide inhaler (20 - 40 μ g tds).
- Oxitropium bromide inhaler.

B) Antihistamines: “ H₁ receptor antagonists ”

- Terfenadine (rarely used).

C) Antileukotrienes:

- Montelukast (Leukotriene receptor antagonist).
- Zileuton (Leukotriene synthesis inhibitor).

Monotherapy in *mild persistent asthma*, Add – on therapy in *moderate to severe asthma*.
Useful in: *aspirin – induced asthma*.

3. ANTI – INFLAMMATORY DRUGS

A) Corticosteroids:

1. Inhaled corticosteroids:

DRUG:

- Beclomethasone (daily dose = see later).
- Fluticasone.
- Budesonide.

SIDE EFFECTS:

- Hoarseness of voice.
- Oropharyngeal candidiasis.

2. Oral corticosteroids:

DRUG:

- Prednisone: 1 mg Kg / day.

SIDE EFFECTS:

- Refer to: Rheumatoid arthritis.

3. Parenteral corticosteroids: (for Status asthmaticus)

DRUG:

- Methylprednisolone.
- Hydrocortisone.

SIDE EFFECTS:

- Refer to: Rheumatoid arthritis.

B) Other anti-inflammatory drugs:

- Gold, Methotrexate, Cyclosporine.
- Under trial for severe chronic asthma not responding to other drugs.

4. PROPHYLACTIC DRUGS

A) Disodium cromoglycate:

- It inhibits release of mediators from mast cells (mast cell stabilizer).
- Dose: inhaled puff = 1 mg, 2 puffs / 6 hours.

B) Kitotifen:

- It inhibits release of mediators from mast cells (mast cell stabilizer).
- It has antihistaminic effect.
- Dose: oral tablet = 1 mg, 1 tablet bid.

C) Omalizumab: (Recombinant Anti – IgE)

- It combines with free IgE blocking its interaction with mast cells.
- Dose: single injection, (SC every 2 – 4 weeks).

3

LONG TERM CONTROL

[STEP THERAPY BASED ON ASTHMA SEVERITY]

Mild Intermittent Asthma

People with mild intermittent asthma do not need daily medication.

QUICK-RELIEVER Short Acting β_2 – Agonist (SABA) (inhaler),

Salbutamol is used:

Only: as needed (up to a maximum of four times / day).

CONTROLLERS: long – term control medicines,

None is needed.

Mild Persistent Asthma

People with mild intermittent asthma need two types of medicines:

QUICK-RELIEVERS: Short Acting β_2 -Agonist (SABA) (inhaler),
Salbutamol is used:

For immediate relief: if an asthma attack occurs.

PLUS

CONTROLLERS: long – term control medicines, [Single drug]

Inhaled corticosteroids (low dose range $\approx 100 - 200 \mu\text{g} / \text{day}$) are used:

As a maintenance every day to prevent symptoms and attacks.

Moderate Persistent Asthma

People with mild intermittent asthma need two types of medicines:

QUICK-RELIEVERS: Short Acting β_2 -Agonist (SABA) (inhaler),
Salbutamol is used:

For immediate relief: if an asthma attack occurs.

PLUS

CONTROLLERS: long – term control medicines, [2 drugs]

Inhaled corticosteroids (medium dose range $\approx 200 - 400 \mu\text{g} / \text{day}$),

Long Acting β_2 -Agonist (LABA) (inhaler), e.g. *Salmeterol*

A combination of these drugs are used:

As a maintenance every day to prevent symptoms and attacks.

Severe Persistent Asthma

People with mild intermittent asthma need two types of medicines:

QUICK-RELIEVERS: short acting bronchodilator (β_2 -stimulant inhaler),
Salbutamol is used:

For immediate relief: if an asthma attack occurs.

PLUS

CONTROLLERS: long – term control medicines, [Multiple drugs]

Inhaled corticosteroids (high dose range $> 400 \mu\text{g} / \text{day}$),

Long Acting β_2 -Agonist (LABA) (inhaler), e.g. *Salmeterol*

Antileukotrienes, e.g. *Zileuton*

A combination of these drugs are used:

As a maintenance every day to prevent symptoms and attacks.

STEP THERAPY BASED ON ASTHMA SEVERITY		
Classification	Quick Relievers	Contollers
<u>STEP 1</u> <i>Mild Intermittent</i>	prn *	None
<u>STEP 2</u> <i>Mild Persistent</i>	prn	<u>[Single drug]</u> (esp. with anti-inflammatory activity) <i>Inhaled corticosteroids</i>
<u>STEP 3</u> <i>Moderate Persistent</i>	prn	<u>[2 drugs]</u> <i>Inhaled corticosteroids,</i> <u>plus</u> <i>LABA inhaler</i>
<u>STEP 4</u> <i>Severe Persistent</i>	prn	<u>[Multiple drugs]</u> <i>Inhaled corticosteroids,</i> <u>plus</u> <i>LABA inhaler</i> <u>plus</u> <i>Antileukotrienes</i>

* prn = pro re nata = as needed

CLINICAL CLASSIFICATION OF DRUGS

1. QUICK-RELIEVERS: used to relieve the **ATTACKS**

- **Short acting Inhaled β_2 agonists (SABA)**
- Inhaled anticholinergics
- Short acting xanthines
- IV corticosteroids

2. CONTROLLERS: used for **MAINTENANCE**

- **Long acting Inhaled β_2 agonists (LABA)**
- **Inhaled corticosteroids & oral corticosteroids**
- **Antileukotrienes**
- Disodium cromoglycate
- Long acting xanthines

4 TTT OF STATUS ASTHMATICUS

A) HOSPITALIZATION: in a respiratory ICU.

B) DRUGS:

1. β_2 - Agonists: “SALBUTAMOL”
 - o IPPB: using Nebulizer, 5 mg with O₂.
OR
 - o Parentral: IV infusion, 250 ug over 10 minutes,
(If no improvement occurs with Nebulizer)
2. Inhaled anticholinergics: “IPRATROPIUM BROMIDE”
 - o IPPB: using Nebulizer, 250 ug with nebulized salbutamol.
3. Aminophylline: (Short acting, continuous IV infusion, rarely used)
 - o Loading dose: 5 mg / kg over 30 minutes.
 - o Maintenance dose: 0.5 mg /kg /hour.

IF THERE IS NO RESPONSE: ADD:

4. Systemic corticosteroids:
 - o Methylprednisolone: 2 mg / Kg IV followed by 1 mg / Kg / 6 hours.
 - o Hydrocortisone: 200 mg IV & repeated / 6 hours.
 - o Oral prednisone: AFTER IMPROVEMENT
1mg / Kg / day orally is given for 2 weeks, **then**
the dose is gradually tapered by 5 mg every 3 days.

C) SUPPORTIVE MEASURES:

1. Oxygen inhalation.
2. Correction of: acidosis, electrolyte imbalance.

D) MECHANICAL VENTILATION:

- May be needed in severe resistant cases.

LUNG COLLAPSE (ATELECTASIS)

DEFINITION

- Deflation of the alveoli → reduced aeration of the lung.

ETIOLOGY

1 Neonatal collapse

1- Congenital (adhesive) collapse:

This is usually due to diminished surfactant.

2- Aspiration:

Aspiration of amniotic fluid or mucus during labour causes lack of aeration of part of the lung.

2 Acquired collapse

1- Obstructive (absorption) collapse: *"The most common"*

- Occurs as a result of: complete bronchial obstruction which is followed by absorption of air from the alveoli into the blood, leading to collapse. No air can get into the lung to replace the absorbed air.
- Causes of bronchial obstruction:
 - In the lumen: *FB or thick secretions.*
 - In the wall: *Tumour.*
 - Pressure from outside: *Tumour, LN.*

Massive post-operative lung collapse

- A very serious example of obstructive collapse, *due to:*
 1. Lack of pre-anaesthetic medication.
 2. Irritation by anaesthetics especially in cases of chronic bronchitis.
 3. Neglected aspiration of secretions following operations.
 4. Inability to cough after operation because of pain.

2- Relaxation-compression collapse:

- In moderate cases of mechanical pressure, e.g. pleural effusion or pneumothorax, the intrapleural pressure rises, becomes less negative, then reaches zero. This causes passive recoil of the alveoli, (relaxation collapse).
- In severe cases, the intrapleural pressure rises more & becomes even positive. This causes compression of the alveoli → more collapse, (compression collapse).

3- Cicatrization collapse:

- Severe parenchymatous fibrosis in a lung area → partial collapse.

CLINICAL PICTURE

Symptoms

1. Symptoms of the cause: e.g. br. carcinoma.

2. Symptoms due to collapse:

A. In most cases:

- Mild cases: *asymptomatic*.
- Severe cases: *dyspnea & may be cyanosis*.

B. In massive post-operative lung collapse: “4 manifestations”

- Acute chest pain.
- Dyspnea (severe) & cyanosis.
- Acute RVF.
- Shock.

2. **Bronchoscopy:**

- Diagnostic: for detection of the cause, e.g. br. carcinoma or FB.
- Therapeutic: for removal of the obstructing material, *if possible*.

DIFFERENTIAL DIAGNOSIS

1. Causes of: “**syndrome of multiple negatives**”
Pleural effusion, lung collapse, lung fibrosis.
2. Consolidation.
3. Differentiation of: “**acute massive post-operative lung collapse**”
 Other causes of: acute chest pain, dyspnea, acute RVF & Shock:
 - Massive myocardial infarction.
 - Massive pulmonary embolism.
 - Tension pneumothorax.

TREATMENT

1. **Treatment of the cause:** e.g.
 - A) Obstructive (absorption) collapse:
 - Bronchoscopic removal of foreign bodies or secretions.
 - The patient is placed on the healthy side & the affected side is heavily percussed to dislodge the obstructing material.
 - B) Relaxation-compression collapse:
 - TTT of the cause: e.g. pleural effusion or pneumothorax.
2. **Treatment of complications:** e.g.
 - Antibiotics for infection.
3. **Oxygen inhalation.**
4. **Respiratory exercises.**

PULMONARY FIBROSIS

TYPES

1 Pulmonary fibrosis

I. Parenchymatous fibrosis:

- Occurs as a complication of various lung diseases, **e.g.**
 - TB.
 - Lung abscess.
 - Bronchiectasis.

II. Interstitial fibrosis: (ILD)

- Occurs in between the alveoli, in the interstitial tissue.

2 Pleuro-Pulmonary fibrosis “ fibrothorax ”

- Pleural diseases may heal by extensive fibrosis that extends to the lung parenchyma.
- It commonly complicates:
 - Hemothorax.
 - Empyema.

Parenchymatous fibrosis & Fibrothorax

CLINICAL PICTURE

Symptoms

1. Symptoms of the cause: e.g. TB toxemia.
2. Symptoms due to fibrosis:
 - Dyspnea.
 - Dry cough.
 - Chest pain (in fibrothorax).

Signs

1. Signs of the CAUSE: e.g. TB.
2. LOCAL signs:

Inspection

- Shape: retraction on the affected side.
- Movement: diminished on the affected side.

Palpation

- **T**rachea & mediastinum: shifted to the same side.
- **T**VF: decreased.

Percussion

- Dullness: patchy (heterogenous).

Auscultation

- Breath sounds: diminished.
- Additional sounds: crepitations.

COMPLICATIONS

1. Bronchiectasis.
2. Cor pulmonale.
3. Cicatrization collapse.
4. Respiratory failure: *in severe bilateral cases.*

INVESTIGATIONS

1. CXR:

A) Features of the CAUSE: e.g. TB.

B) Features of fibrosis:

- Opacity: heterogenous with reticulations.
- The trachea & mediastinum: may be shifted to the same side.
- The copula of the diaphragm: may be elevated (TENTING).

2. Respiratory function tests:

- Evidence of: RESTRICTIVE HYPOVENTILATION.

DIFFERENTIAL DIAGNOSIS

- Causes of: “syndrome of multiple negatives”
Pleural effusion, lung collapse, lung fibrosis.

TREATMENT

- Treatment of the cause, e.g. TB.
- Treatment of the complications, e.g. Respiratory failure.

Interstitial Lung Fibrosis (ILD)

DEFINITION

- Diffuse inflammatory disorders of the lower respiratory tract characterized by:
alveolitis, *thickening of alveolar walls*, *extensive fibrosis* of the interstitial tissue.

ETIOLOGY

1. Idiopathic pulmonary fibrosis (IPF).
2. Immune diseases:
 - Collagen diseases.
 - Good Pasture's syndrome.
3. Inflammatory bowel diseases:
 - Crohn's disease.
 - Ulcerative colitis.
4. Inhalational lung diseases:
 - Extrinsic allergic alveolitis (*due to organic dust*)
 - o Farmer's lung.
 - Pneumoconiosis (*due to inorganic dust*)
 - o Silicosis.
 - o Asbestosis.
5. Iatrogenic:
 - Amiodarone.
6. Hepatic diseases:
 - Chronic active hepatitis.
 - Primary biliary cirrhosis.
7. Heart diseases:
 - Chronic LSHF.
8. SARCOIDOSIS.

PATHOPHYSIOLOGY

- IMPAIRED DIFFUSION (Hypoxia with normocapnea).
- Restrictive hypoventilation.

CLINICAL PICTURE

Symptoms

- Dyspnea (gradual & progressive).
- Dry cough.

Signs

- Central cyanosis.
- Clubbing.
- Crepitations (diffuse).

COMPLICATIONS

1. Respiratory failure.
2. Right ventricular failure (corpulmonale).

INVESTIGATIONS

1. CXR:

- Bilateral diffuse lung affection in the form of:
reticulations & micronodular infiltrations (GGA).
- Pulmonary hypertension $\pm$ right ventricular enlargement.

2. Pulmonary function tests:

- Ventilation tests:
Restrictive hypoventilation.
- Diffusion tests:
Decreased CO transfer factor.

3. Arterial blood gases:

- Hypoxia.
- Normocapnea.

4. Assessment of disease activity: (active alveolitis)

- BAL: for detection of type & amount of inflammatory cells in active alveolitis.
- Gallium-67 scan:
 - o The affected lung tissue (with active alveolitis) takes up Gallium-67.
 - o The normal lung tissue does not take up Gallium-67.
- Open lung biopsy: for detection of active alveolitis.

5. Investigations for the cause.

TREATMENT

1. Treatment of the cause.
2. Treatment of Idiopathic Pulmonary Fibrosis:
 - o Corticosteroids: prednisone: 1 mg / kg / day.
 - o Cytotoxic drugs: e.g. cyclophosphamide.
3. Symptomatic treatment:
 - o Oxygen therapy.
4. Treatment of complications:
 - o Respiratory failure.
 - o Right ventricular failure.

COR PULMONALE

DEFINITION

Right ventricular hypertrophy with or without failure, resulting from PH, due to: parenchymal or vascular lung disease.

ETIOLOGY

A) Acute cor pulmonale:

1. Massive pulmonary embolism.
2. Tension pneumothorax.
3. Massive lung collapse.

B) Subacute cor pulmonale:

1. Lymphagitis carcinomatosa.
2. Recurrent showers of pulmonary emboli.

C) Chronic cor pulmonale:

1. Hypoxic cor pulmonale:

Occurs in almost all cases of chronic lung diseases, **e.g.**

- Obstructive hypoventilation **e.g.** COPD.
- Restrictive hypoventilation **e.g.** ILD.

2. Vascular cor pulmonale:

- Primary pulmonary hypertension.
- Pulmonary bilharziasis.
- Pulmonary vasculitis.
- Sickle cell anemia.
- Recurrent showers of pulmonary emboli.

CLINICAL PICTURE

- 1- Features of: the cause.
- 2- Features of: pulmonary hypertension.
- 3- Features of: right ventricular enlargement.
- 4- May be features of: right ventricular failure.

INVESTIGATIONS

1. CXR:

- Features of: the cause.
- Features of: pulmonary hypertension.
- RV enlargement.
- RA enlargement.

2. ECG:

- RV enlargement.
- RA enlargement (p – pulmonale).

3. Echocardiography:

- RV enlargement.
- RA enlargement.

TREATMENT

- 1- Treatment of the cause.
- 2- Treatment of pulmonary hypertension: (Refer to Cardiology).
- 3- Treatment of right-sided heart failure: (Refer to Cardiology).

HYPOXIC VERSUS VASCULAR COR PULMONALE

	Hypoxic cor pulmonale	Vascular cor pulmonale
Dyspnea	Marked	Minimal or absent
Sputum	Mucopurulent	Absent
Cyanosis	Central due to hypoxia	Peripheral due to low CO
Clubbing	Common	Absent
<u>Chest Examination</u> • <i>Shape</i> • <i>Breath sounds</i> • <i>Additional sounds</i> • <i>Features of PH</i>	Barrel –shaped Prolonged expiration Wheezes May be masked	Normal Normal Absent Marked
<u>ABG</u>	Hypoxia, may be hypercapnia	Usually normal

Bilharzial Cor Pulmonale

ETIOLOGY

1. Schistosoma mansoni ova:

- They reach the lungs only in the presence of portal hypertension and porto-systemic shunts which allow the ova to bypass the liver to the lungs.
- They cause more destructive lesions than *S. haematobium*.

2. Schistosoma haematobium ova:

- They reach the lungs more commonly since the worms live in the pelvic venous plexuses which drain into the IVC, then to the lungs.
- They usually produce mild lesions.

PATHOLOGY

1. Pulmonary hypertension:

- The bilharzial ova reach the lungs as emboli leading to necrotising arteriolitis due to the secretion of miracidial toxins. This is followed by:
end-arteritis obliterans with obliteration of pulmonary arterioles leading to: pulmonary hypertension.
- *Bilharzial immune complexes* may play a role through causing pulmonary vasculitis, leading to pulmonary hypertension.

2. Cor pulmonale:

- Pulmonary hypertension → RVH & eventually RVF (cor pulmonale).

3. Aneurysm formation:

- Aneurysmal dilatation of the pulmonary artery & its two main branches occur due to progressive weakness in the wall of the arteries.

CLINICAL PICTURE

Symptoms

- Symptoms of: low CO.
- Symptoms of: RVF may occur lately.
- No central cyanosis.

Signs

- Signs of: pulmonary hypertension.
- Signs of: right ventricular enlargement.
- Signs of: RVF may occur lately.
- Signs of: PULMONARY ANEURYSM:
“marked pulsations & dullness in the left second left space”.
- Hepatosplenomegaly & signs of portal hypertension.

INVESTIGATIONS

1. CXR:

- Marked dilatation of the main pulmonary arteries forming:
“ Dumb-bell shaped shadows in the hila ”.
- Peripheral pulmonary oligemia.
- RV enlargement.
- RA enlargement.

2. ECG:

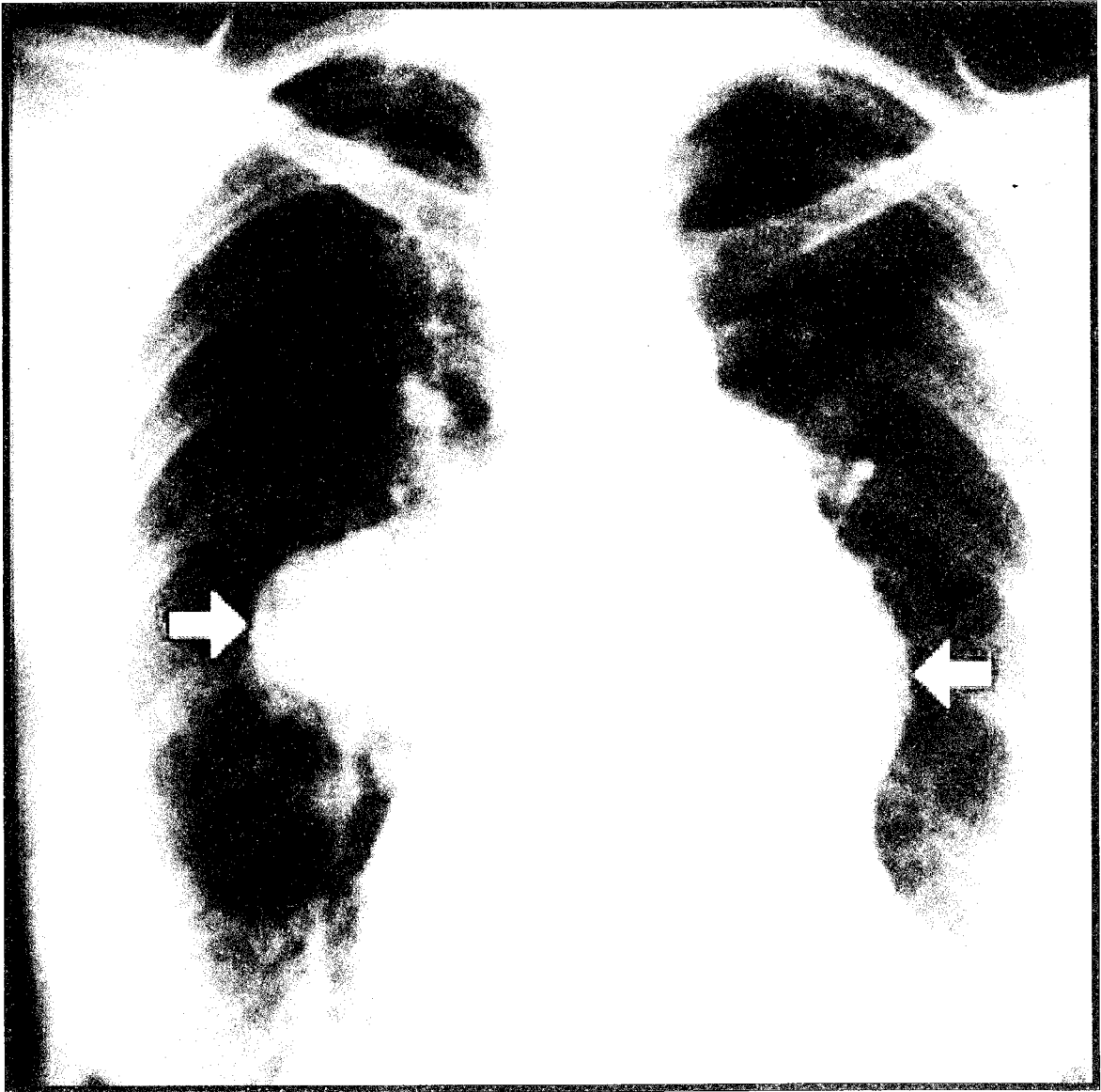
- RV enlargement.
- RA enlargement (p – pulmonale).

3. Investigations for bilharziasis: (refer to GIT).

TREATMENT

- 1) Proper treatment of cor pulmonale.
- 2) Anti-bilharzial treatment.

Marked dilatation of the main pulmonary arteries forming:
“ Dumb-bell shaped shadows in the hila ”



TUBERCULOSIS

DEFINITION

- It is a common contagious infection caused by MYCOBACTERIUM TB.
- It primarily affects the LUNGS, however: infection can spread to other organs.

ETIOLOGY

1. Causative organism:

MYCOBACTERIUM TB

- **A**cid – fast.
- **A**lcohol – fast.
- **A**erobic.

2. Source of infection:

- Patients with **A**ctive pulmonary TB, especially with cavitary lesion.

3. Mode of infection:

- **A**irway Droplet infection, especially with prolonged contact (weeks).

PREDISPOSING FACTORS

1. Age:

- Below 5 y: High susceptibility to infection.
- 5 – 15 y: Less susceptibility (golden age).
- Above 15 y: High susceptibility to progressive pulmonary disease.

2. Race: more common in black races.

3. Incidence: “Poor countries & Poor socio-economic classes”

- **P**oor nutrition, **P**oor hygienic conditions.

4. Occupation:

- **P**aramedical & medical people are more exposed to infection.

5. Chest diseases:

- **P**neumoconiosis: e.g. Silicosis, asbestosis ↓ resistance to infection.
- **P**ulmonary oligoemia: e.g. PS.

6. Decreased immunity:

- **D**iabetes mellitus.
- **D**rugs: *Corticosteroids & other immunosuppressives.*
- **A**IDS.
- **M**alignancies, *especially lymphomas.*
- **M**alnutrition.

PATHOGENESIS

I. ENTRY

Inhaled TB bacilli travel via the airways to be deposited in the pulmonary parenchyma, especially in the upper zones, probably due to high O₂ tension which favours the growth of the organisms.

II. FIGHT

Alveolar macrophages ingest TB bacilli & try to phagocytize them.

Alveolar macrophages usually fail to completely destroy the bacilli which possess natural defences. They are usually not destroyed.

There is a fight between the: Alveolar macrophages & TB bacilli.

III. FATE

1. Primary TB: (Childhood)

a) Latent form:

In most immunocompetent individuals, macrophages are successful in inactivating the bacilli. The bacilli stay: LATENT or DORMANT.

Therefore the infection is self-limited and often subclinical.

Patients are asymptomatic: and the underlying lung pathology is:

The primary complex: Gohn's focus, regional lymphadenitis, lymphangitis

b) Active (Progressive) form:

In some patients, macrophages fail to inactivate the bacilli.

The bacilli become active leading to a clinically apparent infection.

Patients may present with: pulmonary or extrapulmonary manifestations

2. Postprimary (reactivation) TB: (Adulthood)

After a period of latent primary TB, reactivation of the disease may occur at any time if the immunity of the patient drops.

Patients may present with: pulmonary or extrapulmonary manifestations

PATHOLOGY

1. Primary TB: (Childhood)

a) Gohn's focus: (pulmonary component)

An area of consolidation formed by aggregation of tubercles, present usually in the mid to upper zones, usually supleural.

b) Regional lymphadenitis (glandular component)

c) Lymphangitis in the intervening lymphatic vessels.

2. Postprimary (reactivation) TB: (Adulthood)

a) Gross:

- This depends on the state of immunity & the virulence of the organism:

1. FIBROCASEOUS TB:

- Big **cavity** surrounded by little fibrosis.

2. FIBROID TB:

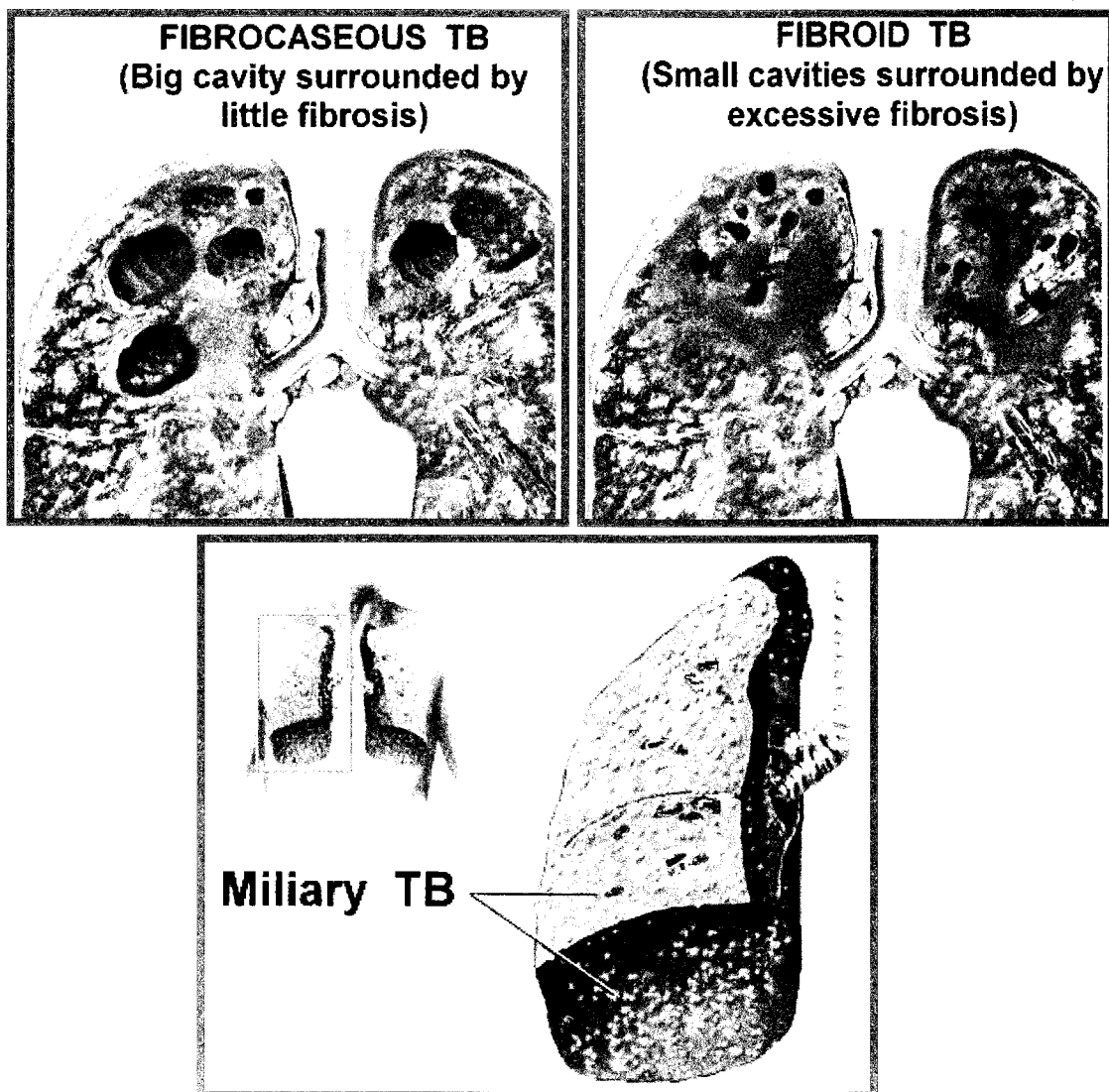
- Small cavities surrounded by excessive **fibrosis**.

3. Endobronchial TB:

- TB bronchitis of the bronchi connected to TB cavities.

4. TB bronchopneumonia & Miliary TB:

- These types occur in immunocompromised patients.



b) Microscopic:

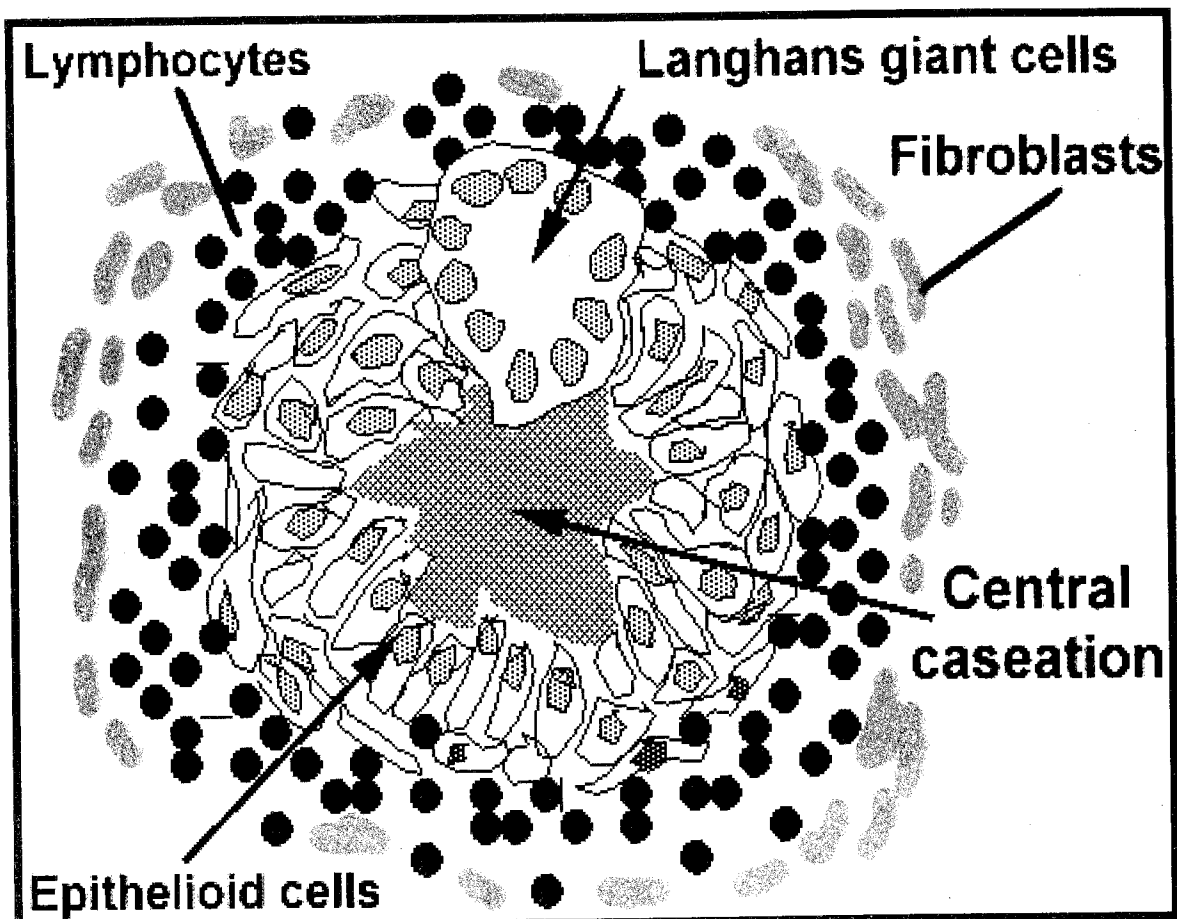
- The characteristic lesion is: “Typical TB granuloma”

o CASEATION: central, surrounded by:

o CELLS:

- *Lymphocytes.*
- *Langhans giant cells.*
- *Epithelioid cells.*
- *Fibroblasts.*

o CALCIFICATION.



Typical TB granuloma

CLINICAL TYPES

1. Primary TB:

(Childhood)

a) Latent form:

Patients are usually asymptomatic.

b) Active (Progressive) form:

Patients may present with: pulmonary or extrapulmonary manifestations

2. Postprimary (reactivation) TB:

(Adulthood)

a) PULMONARY TB.

b) EXTRA – PULMONARY TB.

PULMONARY TB

CLINICAL PICTURE

Symptoms

1. General symptoms:

- a) Chronic presentation: “ Symptoms of TB toxemia ”
- **Night** sweat.
 - **Night** fever.
 - *Loss* of weight.
 - *Loss* of appetite.
- b) Acute presentation:
- Flu-like or Typhoid-like presentation.

2. Chest symptoms:

- a) Cough:
- With expectoration of a mucopurulent sputum.
 - Which may be rarely coin-shaped (nummular sputum).
- b) Hemoptysis: (Common: Frank or Blood – tinged)
- Bleeding from vascular granulation tissue.
 - Bleeding due to erosion of a big vessel crossing a TB cavity.
- c) Dyspnea: due to any lung pathology, especially:
- Consolidation, cavitation, fibrosis or pleural effusion.
- d) Chest pain: due to:
- Pain in the intercostals muscles from *chronic cough*.
 - Pneumothorax.
 - Pleurisy.

Signs

1. General signs:

- Fever, toxic facies, loss of weight.
- Clubbing: in advanced untreated cases with severe toxemia.
- PALLOR.

2. Chest signs: (variable depending on the lesion)

- Apical: *cavitation*, *fibrosis*. (the most common)
- Others: consolidation,
 bronchopneumonia, bronchiectasis,
 pleural effusion, pneumothorax.

COMPLICATIONS

1. AMYLOIDOSIS (Secondary).
2. Aspergilloma (formed in a TB cavity).
3. SPREAD (Extra – pulmonary TB).
4. COMPLICATIONS OF ANTI – TB drugs.

INVESTIGATIONS

I. LABORATORY INVESTIGATIONS

1. General: (evidence of tissue inflammation)

- a) ESR: markedly elevated.
- b) CRP: elevated.
- c) CBC:
 - o WBCs: lymphocytosis & monocytosis.
 - o RBCs: anemia.

2. Bacteriology:

- a) Sputum: for TB bacilli
 - *Staining:* ZN stain.
 - *Culture:* Lowenstein-Jensen medium or BACTEC.
 - *Animal Innoculation:* Guinea pig.
- b) BAL: for TB bacilli (if no sputum is available).

3. Tuberculin test: (Mantoux test)

a) Method:

- Injection of 0.1 cc of 1/10,000 PPD (Purified Protein Derivative).
ID in the upper part of the front of the forearm.
- The result is recorded after 72 hours.
- **Positive tuberculin:** indurated area of 1 cm or more in diameter.

b) Values:

1. Positive test indicates:
 - Infection with TB (whether *active* or *old*).
2. Positive test in children below 3 years usually indicates:
 - *Active* infection.
3. Negative test usually indicates:
 - Absence of infection with TB.
4. Negative test in adults susceptible to infection (Med, Paramed) indicates:
 - The need for BCG vaccination.

c) False positive tuberculin test:

1. Atypical mycobacteria.
2. Nocardia.
3. PREVIOUS BCG VACCINATION.

d) False negative tuberculin test:

1. Fulminant cases, e.g. acute miliary TB.
2. Decreased immunity: Lymphoma, AIDS, Corticosteroids.
3. Inactive tuberculin.

4. PCR: (*Polymerase Chain Reaction*)

- For detection of: *Mycobacterial DNA*.

II. IMAGING

1. CXR:

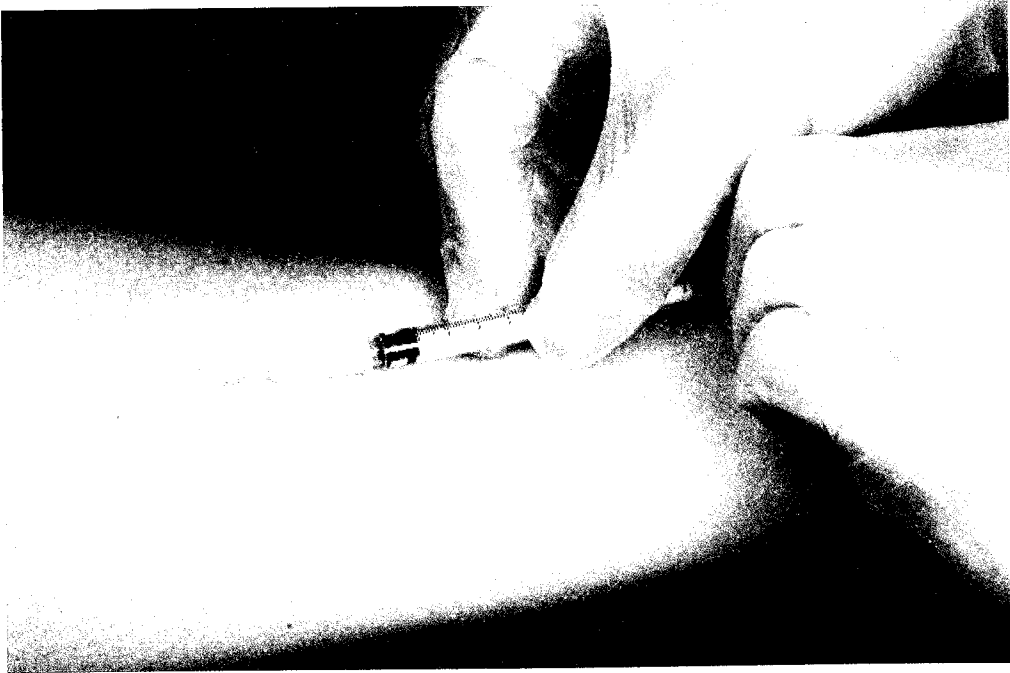
- Radiologic findings are more prominent in the upper lung zones.
- Radiologic findings are variable depending on the lesion:
 1. Fibrocaceous TB: apical cavities surrounded by opacities.
 2. TB bronchopneumonia: irregular patches scattered in the lungs.
 3. Miliary TB: numerous small shadows of equal sizes (GGA).
 4. Others:
 - *Fibrosis.*
 - *Calcification.*
 - *Enlarged hilar LN.*
 - *Pleural effusion.*

2. CT scan.

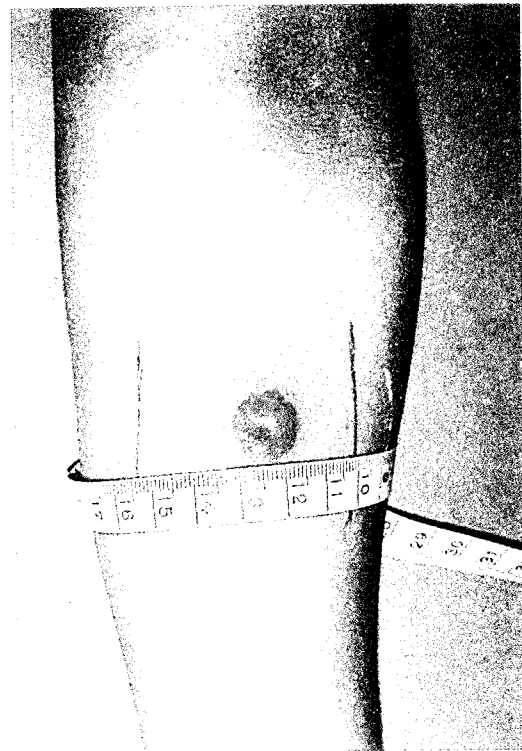
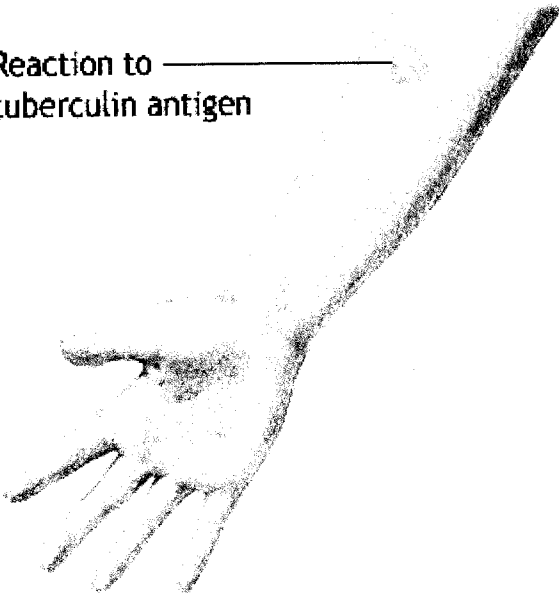
III. BIOPSIES (Transbronchial, Pleura, LN):

- “Typical TB granuloma” (see before).

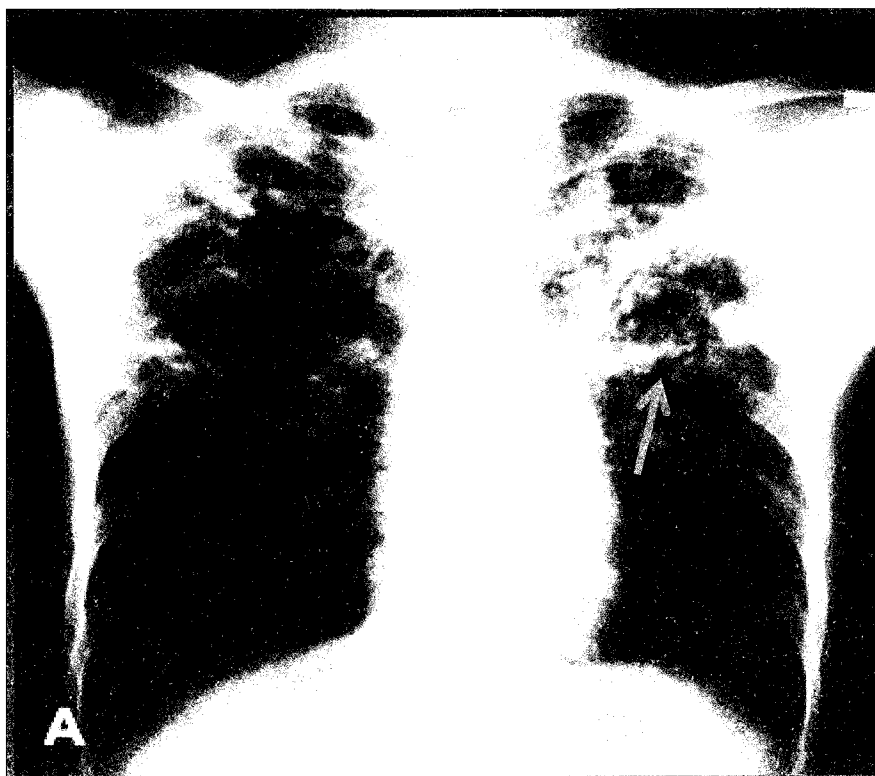
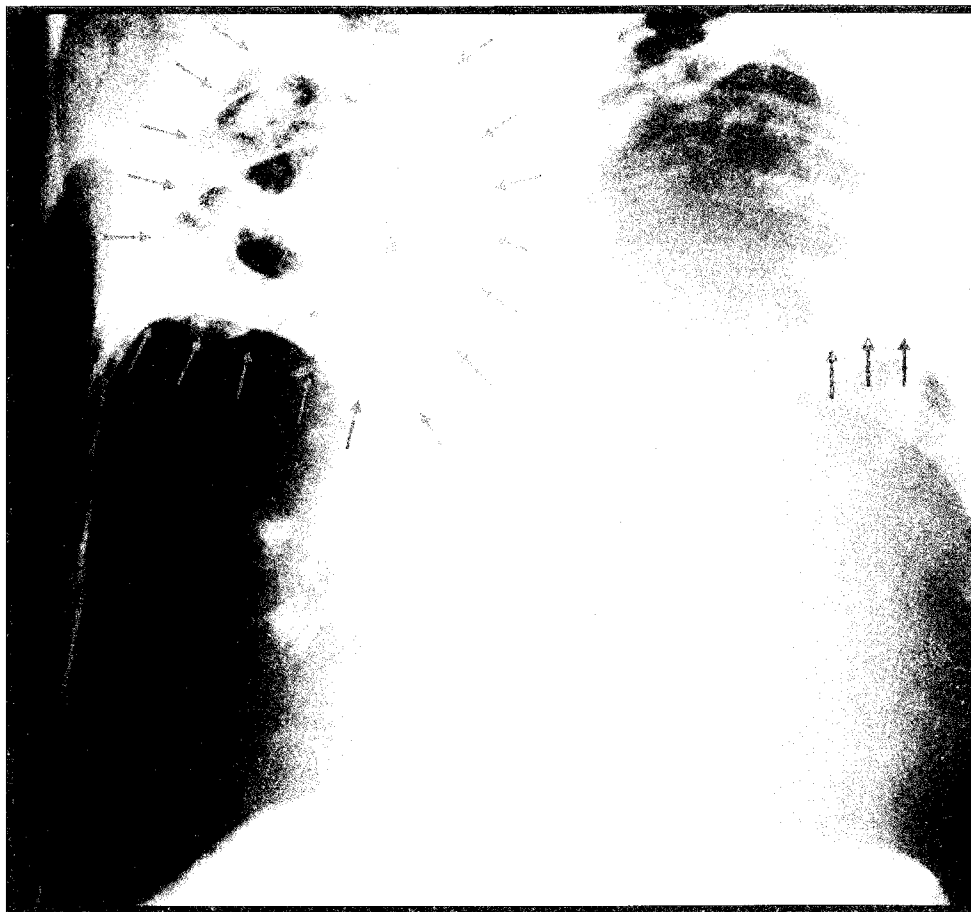
Tuberculin test



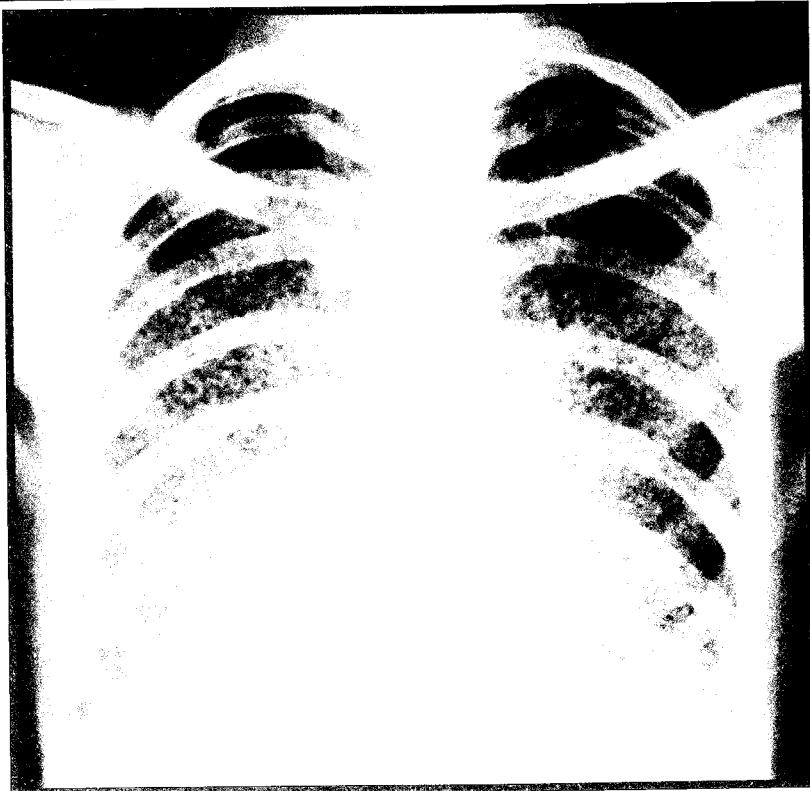
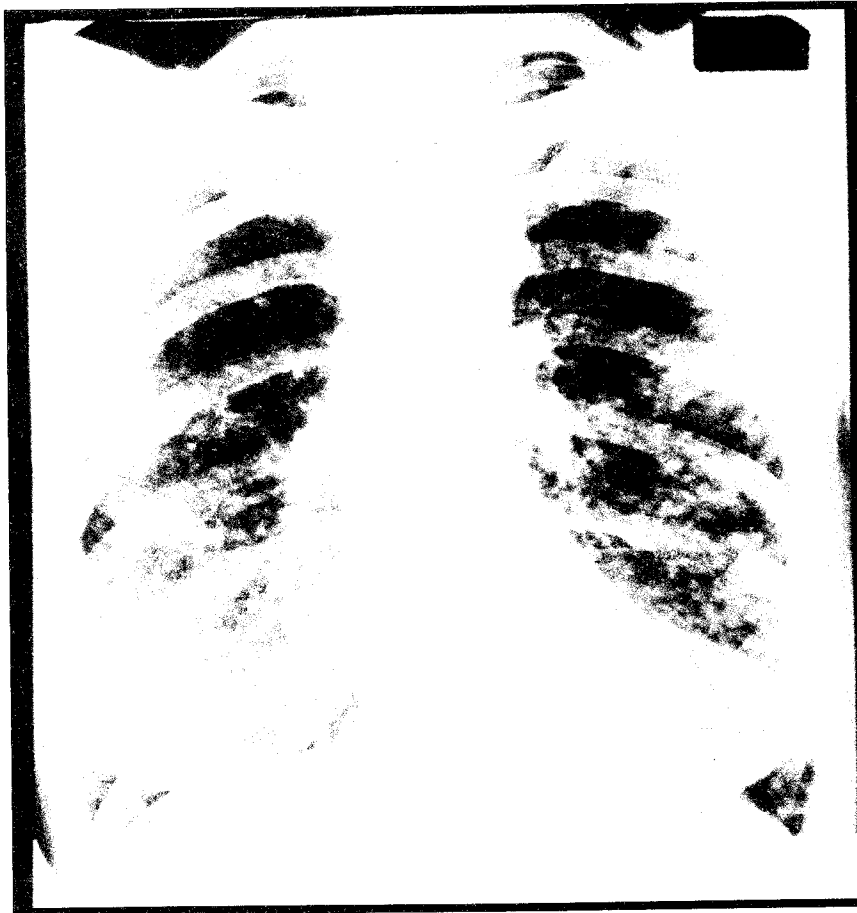
Reaction to _____
tuberculin antigen



Apical cavitation surrounded by some fibrosis



Miliary TB (GGA)



EXTRA – PULMONARY TB

- It occurs due to Hematogenous spread of TB bacilli from:
 1. Primary TB: from the *pulmonary or glandular component*.
 2. Postprimary TB: from the *pulmonary lesion*.

CLINICAL PICTURE

Single organ affection

1. Thoracic:

- a) Heart: e.g. pericardial effusion, constrictive pericarditis.
- b) Mediastinum: e.g. TB lymphadenitis.
- c) Chest wall: e.g. ribs (osteomyelitis).

2. Extra - Thoracic:

- a) Lymphatic:
 - TB lymphadenitis.
- b) CNS:
 - TB meningitis.
 - Tuberculoma.
- c) Abdominal:
 - TB enteritis: commonly in the ileocecal region.
 - TB peritonitis.

d) Genitourinary:

- Urinary: *Kidneys, ureter, UB.*
- Male genital: *Prostate, epididymis, seminal vesicles.*
- Female genital: *Uterus, ovaries, Fallopian tubes.*

e) Skeletal:

- TB osteomyelitis.
- TB arthritis.
- POTT'S DISEASE OF THE SPINE.

f) OTHERS:

- Adrenals: Addison's disease.
- Skin: Lupus vulgaris.

Miliary TB

1. General systemic manifestations:

- Fever, CYANOSIS, toxic facies, loss of weight, anorexia, sweats.

2. Chest manifestations:

- Cough, dyspnea, generalized crepitations.

3. Other manifestations:

- HSM, Meningitis, Polyserositis, EYE (choroid tubercles).

INVESTIGATIONS OF MILIARY TB

1. Tuberculin test: may be false negative.
2. CXR: numerous small shadows of equal sizes (GGA).
3. BIOPSY: transbronchial, liver, BM.

TREATMENT

I. Prophylactic

1. Early diagnosis: (for high risk groups, e.g. Med & Paramed)
 - Mass radiography.
 - Tuberculin survey.
 - Sputum examination.
2. Immunoprophylaxis: (for high risk groups, e.g. Med & Paramed)
 - BCG vaccination.
3. Chemoprophylaxis: (for contacts of tuberculous patients)
 - INH.

II. Therapeutic

1. General measures

- Proper nutrition.
- Rest in bed: *in acute cases.*
- Drugs: *antipyretics, expectorants, mucolytics.*

2. Specific measures

“Chemotherapy”

A) Plan of therapy:

1. Combined drug therapy is needed to:
 - Overcome natural resistance to anti – TB drugs.
 - Accelerate mycobacterial clearance.
2. Long duration of therapy is needed especially in:
 - Extrapulmonary TB.

B) Anti-Tuberculous drugs:

1. Isoniazid (INH):

Dose:

- 5 mg / Kg / day *orally*.

Side effects:

- LIVER: Hepatotoxicity (**CAH**).
- NEUROLOGICAL:
 - PN (mainly sensory, **give B6**).
 - Psychosis & epilepsy.
- LUPUS – LIKE manifestations.

2. Rifampicin:

Dose:

- 10 mg / Kg / day *orally*.

Side effects:

- LIVER: Hepatotoxicity.
- GIT: irritation.
- URINE: red colouration.

3. Streptomycin:

Dose:

- 15 mg / Kg / day

IM.

Side effects:

- RENAL: Nephrotoxicity.
- OTOTOXICITY: vertigo, deafness.
- NEUROLOGICAL: ataxia, nystagmus.

4. Ethambutol:

Dose:

- 25 mg / Kg / day *orally*.

Side effects:

- EYE: optic neuritis.

5. Pyrazinamide:

Dose:

- 30 mg / Kg / day *orally*.

Side effects:

- LIVER: Hepatotoxicity.
 - METABOLIC: Hyperuricemia.
-

6. Ethionamide:

Dose:

- 1 gm / day *orally*.

Side effects:

- LIVER: Hepatotoxicity.
- GIT: irritation.

7. Cycloserine:

Dose:

- 1 gm / day *orally*.

Side effects:

- NEUROLOGICAL: dizziness, depression.

8. Para-aminosalicylic acid (PAS):

Dose:

- 10 gm / day *orally*.

Side effects:

- GIT: irritation.
- HYPERSENSITIVITY: e.g. skin rash.

9. Capreomycin, Kanamycin, Amikacin:

Dose & side effects: as streptomycin.

C) Regimens:

1. Short regimen: (9 – 12 months)

- INH & Rifampicin: for 9 – 12 months.
- plus:
- Ethambutol or Streptomycin: for the first 2 months only.

2. Very short regimen: (6 months)

- INH & Rifampicin: for 6 months.
- plus:
- Ethambutol or Streptomycin: for the first 2 months only.
- plus:
- Pyrazinamide: for the first 2 months only.

3. Classic regimen: (Rarely used now: 15, 18 or 24 months)

- INH & Rifampicin: for the whole duration.
- plus:
- Ethambutol or Streptomycin: for the first 2 months only.

D) Indications of corticosteroids in TB:

- Corticosteroids are given under cover of anti- TB drugs in:
 1. TB meningitis.
 2. TB serositis (pericardial, pleural, peritoneal).
 3. TB adrenal glands (*replacement therapy*).
 4. Fulminant cases, *e.g. miliary TB.*

3. Surgery: (resection)

- Tuberculoma.
- Destroyed tuberculous lobe.

4. Collapse therapy.

List of famous TB victims

Writers and poets

- **Honoré de Balzac**
- **Emily Brontë**
- **Anton Chekhov**
- **Franz Kafka** (1883-1924), German-language novelist best known for his novel *The Metamorphosis*.
- **Molière**
- **Jean-Jacques Rousseau**
- **Voltaire**

Composers

- **Frédéric Chopin** (1810-1849). Historical records indicate episodes of hemoptysis during performances.
- **Niccolò Paganini**

Leaders and politicians

- **Simón Bolívar**, considered the liberator of several South American countries, died in 1830.
- **Louis XIII of France**
- **Louis XVII of France**
- **Napoleon II of France**
- **Eleanor Roosevelt**

Others

- **Alexander Graham Bell**
- **Vivien Leigh**
- **Tom Jones**

BRONCHOGENIC CARCINOMA

INCIDENCE

- The most common malignant tumour in ♂ in most of the world.
 - More common in males (*due to smoking*).
 - More common between 50 & 70 years of age.

PREDISPOSING FACTORS

1) Cigarette smoking:

- 90 % of cases are caused by smoking cigarettes.
- Quantity X duration = Pack X years (*both are risk factors*).

2) Occupational exposure: (miners)

- Asbestos, nickel, uranium.

3) Chronic lung inflammation, e.g.

- Interstitial fibrosis.

PATHOLOGY

Types

"Histological classification"

1) Small cell carcinoma (oat cell carcinoma) 20 %

- Highly malignant & rapidly growing.
- The most common to produce paraneoplastic syndrome.

2) Non – Small cell carcinoma

a) Squamous cell carcinoma: 40 %

b) Large cell carcinoma: 15 %

c) Adenocarcinoma: 25 %

○ Most common in: asbestos exposure, non-smokers, ♀.

d) Alveolar cell (bronchiolar) carcinoma: 1 %

○ Low grade carcinoma that presents as an alveolar infiltrate.

Site

- Bronchogenic carcinoma is divided according to its site of origin into:

	Central (hilar)	Peripheral
<i>Incidence</i>	More common	Less common
<i>Type</i>	Squamous cell carcinoma	Adenocarcinoma Large cell carcinoma
<i>Spread</i>	To mediastinum early	To pleura early
<i>Clinical picture</i>	cough, hemoptysis dyspnea, chest pain	pleurisy
<i>Bronchoscope</i>	Easily visible	Hardly visible

- Pancoast tumour is an apical peripheral carcinoma.

SPREAD

1) Direct:

- Other parts of the lung.
- Pleura & mediastinum.
- Ribs & vertebrae.

2) Lymphatic:

- Hilar & mediastinal lymph nodes.
- Cervical, axillary, abdominal lymph nodes.

NB Retrograde spread along the lung lymphatics may occur leading to lymphangitis carcinomatosa which may lead to subacute cor pulmonale.

3) Blood:

- Liver.
- Brain.
- Bones.

CLINICAL PRESENTATIONS

1) ASYMPTOMATIC PRESENTATION

- There are no symptoms.
- A coin shadow may be discovered accidentally on: CXR.

2) CHEST PRESENTATIONS

A) Broncho-pulmonary presentations

1. Cough & hemoptysis.
2. Bronchial obstruction:
 - a- Partial:
 - Localised wheeze persistent after cough.
 - Localised bronchiectasis.
 - b- Complete:
 - Collapse: which may be complicated by lung abscess.
3. Pneumonia: *unresolving, or recurrent*.
4. Lung abscess: *due to*:
 - Secondary infection in a collapsed area.
 - Breakdown of the tumour.

B) Thoracic inlet or superior sulcus syndrome

- In cases of pancoast tumour, & manifestations are due to involvement of:
 1. The lower trunk of the brachial plexus, causing:
 - o Pain along the medial aspect of the arm, forearm & hand.
 - o Weakness & wasting of the small muscles of the hand.
 2. The sympathetic chain, causing:
 - o Horner's syndrome.
 3. The blood vessels at the root of the neck, causing:
 - o Arterial obstruction: Unequal pulse & BP in the ULs.
 - o Venous obstruction: Congested non-pulsating NVs, and dilated veins on the chest wall.

C) Pleural presentations

1. Dry pleurisy:

- Due to irritation or infiltration of the pleura.

2. Pleural effusion: “of different types”

- Exudate** (Malignant effusion) **the most common type**
 - Massive, bloody.
 - Rapidly re-accumulates after aspiration, contains malignant cells.
 - May be: mediastinal shift to the same side (due to underlying collapse).
- Transudate:**
 - Due to obstruction of the SVC or the azygos vein.
- Chylous effusion:**
 - Due to obstruction of the thoracic duct.
- Suppurative effusion:** (Empyema)
 - Due to rupture of lung abscess into the pleura.

D) Mediastinal presentations

- The patient may present with features of “Mediastinal syndrome” due to:
 - Direct effect of the tumour.
 - Mediastinal lymph node metastasis.
- **e.g.** Phrenic nerve → Diaphragmatic paralysis, RLN → Hoarseness of voice.

3) METASTATIC PRESENTATIONS

a. Direct metastasis:

- Mentioned before.

b. Lymphatic metastasis:

- Mentioned before.

c. Blood metastasis:

- Liver: enlarged, tender, hard, irregular.
- Brain: ↑ ICT & focal neurological manifestations.
- Bones: bony pains & pathological fractures.

4) **NON-METASTATIC PRESENTATIONS**

“Paramalignant syndrome”

- **Definition:**

A group of manifestations that occur as a consequence of the presence of tumour in the body, but not due to the local presence of tumour cells.

- **Incidence:** occur most commonly with **small cell carcinoma**.

- **Underlying mechanisms:** not so clear, however, proposed explanations are:

- Production of abnormal metabolites by tumour cells (cytokines or hormones).
- Immune response against the tumour.

- **Manifestations:**

1. **Neurological:**

- CNS: Encephalomyelitis, Subacute cerebellar degeneration.
- PNS:
 - PN: Peripheral neuropathy.
 - NMJ: Myasthenia gravis, Lambert-Eaton syndrome.
 - Muscles: Secondary myopathy, Dermatomyositis.

2. **Endocrinal:** “due to production of ectopic hormones”

- Pseudohyperparathyroidism.
- Hypoglycemia.
- Cushing’s syndrome.
- SIADH
- Gynecomastia.

3. **Hematological:**

- Granulocytosis: due to the production of **G-CSF**.

4. **Dermatological:**

- Dermatomyositis.
- Acanthosis nigricans.
- Herpes zoster.
- Hyperpigmentation.
- Pruritus.

5. **Others:**

- Clubbing.
- Cachexia.
- Fever not related to infection.

INVESTIGATIONS

1) IMAGING

A) CXR: *

- It detects only tumours bigger than 2 cm in size.
- It may show:
 - Lung:
 - Mass: Coin shadow, or big mass, or apical mass (pancoast).
 - Complication: Pneumonia, lung abscess, or collapse.
 - Pleura:
 - Pleural effusion, with mediastinal shift to the same side.
 - Mediastinum:
 - Mediastinal mass: it could be the tumour itself or its LN.
 - Diaphragm: (Paralysis)
 - Elevated copula on the affected side.
 - Paradoxical movement on the screen.
 - Chest wall:
 - Erosion of the ribs or vertebrae.

B) CT chest:

- It is very accurate & sensitive in detecting the tumour.
- It can detect small tumours (< 2 cm in size) that do not appear on CXR.

2) BRONCHOSCOPY

- Visualization & localization of the tumour, especially the central type.
- Biopsy: could be taken for pathological examination.
- BAL: could be obtained & examined for malignant cells.

* See different CXR figures of bronchogenic carcinoma

3) **CYTOLOGY** “for detection of malignant cells”

1. Sputum examination: may be positive for malignant cells.
2. Aspiration of pleural effusion: may be positive for malignant cells.
3. **BIOPSY**:
 - o *Transbronchial*: through bronchoscopy.
 - o *Lung biopsy*: open, percutaneous, or thoracoscopy.
 - o *Lymph node biopsy*: from enlarged LN.

4) **LABORATORY INVESTIGATIONS**

- CBC: anemia, granulocytosis.
- ESR: elevated (markedly).
- Investigations for diagnosis of endocrinal disturbances: e.g.
 - o *Serum Ca*: for pseudohyperparathyroidism.
 - o *Serum glucose*: for hypoglycemia.
 - o *ACTH*: for Cushing's syndrome.

DIFFERENTIAL DIAGNOSIS

A) **Clinically**:

- The possibility of bronchogenic carcinoma: should be considered in any:
Old, chronic heavy smoker, male: with a chest complaint.
- The DD of bronchogenic carcinoma includes:
 1. Other causes of prolonged cough or hemoptysis.
 2. Other causes of localized bronchial obstruction.
 3. Unresolving pneumonia or lung abscess.
 4. Other causes of pleural effusion.
 5. Other causes of mediastinal syndrome.
 6. **TB**.

B) Radiologically:

- From other causes of **solitary pulmonary shadow** (*coin shadow*):
 1. Pulmonary tumours:
 - Benign tumour.
 - Malignant tumour.
 - Solitary metastasis.
 2. Pulmonary infections, e.g.
 - Pneumonic patch.
 - TB.
 3. Pulmonary infarction.
 4. Foreign body.

TREATMENT

- **Successful surgery offers the only chance of complete cure.**
- **Choice of treatment depends on:**
 1. Histological type of the tumour.
 2. Operability:
 - o No evidence of hilar or mediastinal involvement.
 - o No evidence of extra-thoracic spread.
- **Lines of treatment include:**
 1. For non-small cell carcinoma:
 - A) Operable:
 - Pneumonectomy or lobectomy: may be followed by postoperative irradiation.
 - B) Non-operable:
 - Chemotherapy & palliative radiotherapy.
 2. For small cell carcinoma:
 - Chemotherapy: e.g. cyclophosphamide.
 - Radiotherapy: for treatment of the primary tumour & prophylaxis against metastases.

Neurological manifestations of bronchogenic carcinoma

1) CHEST PRESENTATIONS

Thoracic inlet or superior sulcus syndrome:

- In cases of pancoast tumour, & manifestations are due to involvement of:

1. The lower trunk of the brachial plexus, causing:
 - Pain along the medial aspect of the arm, forearm & hand.
 - Weakness & wasting of the small muscles of the hand.
2. The sympathetic chain, causing:
 - Horner's syndrome.

Mediastinal presentations:

- Phrenic nerve → Diaphragmatic paralysis.
- RLN → Hoarseness of voice.

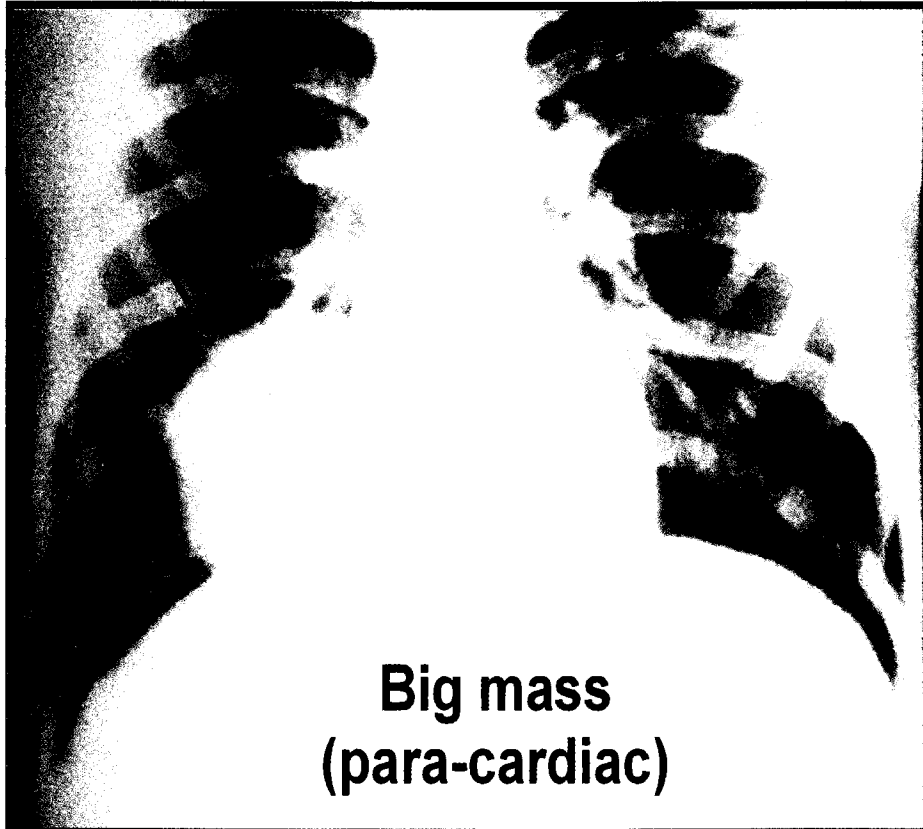
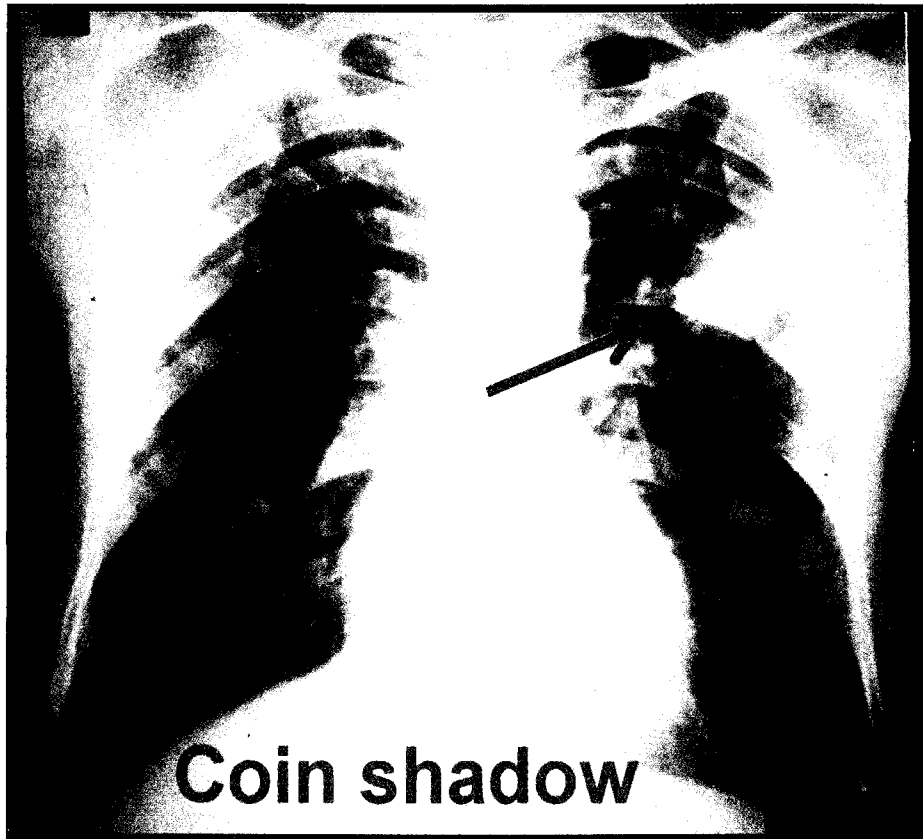
2) METASTATIC PRESENTATIONS

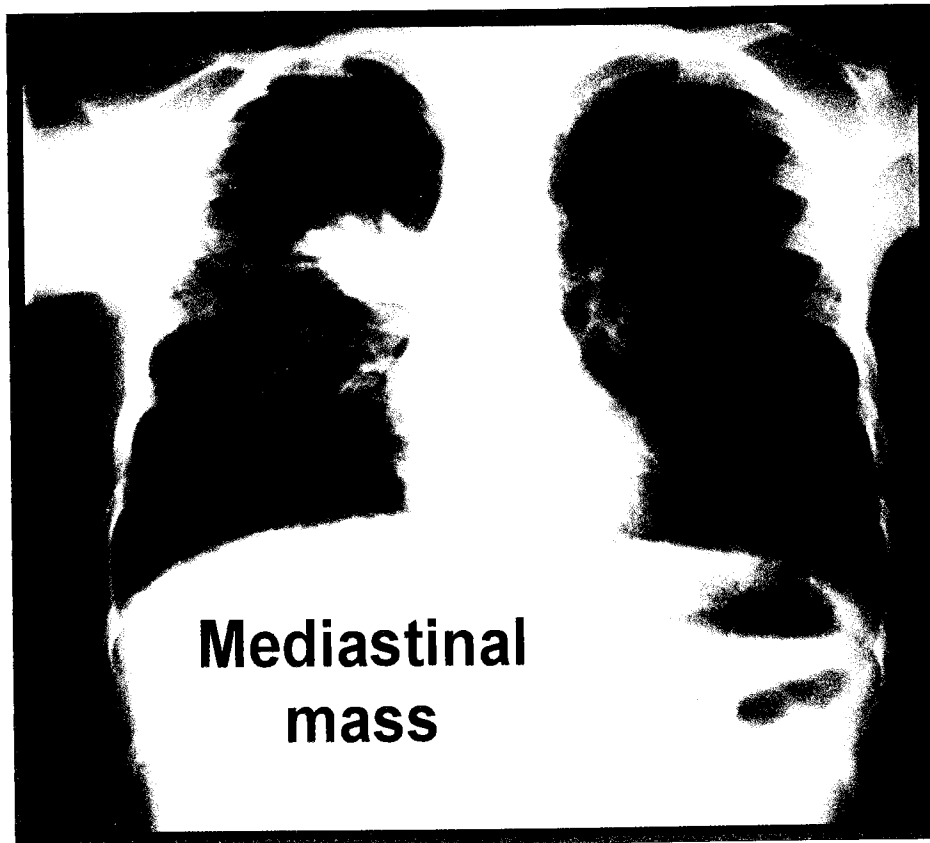
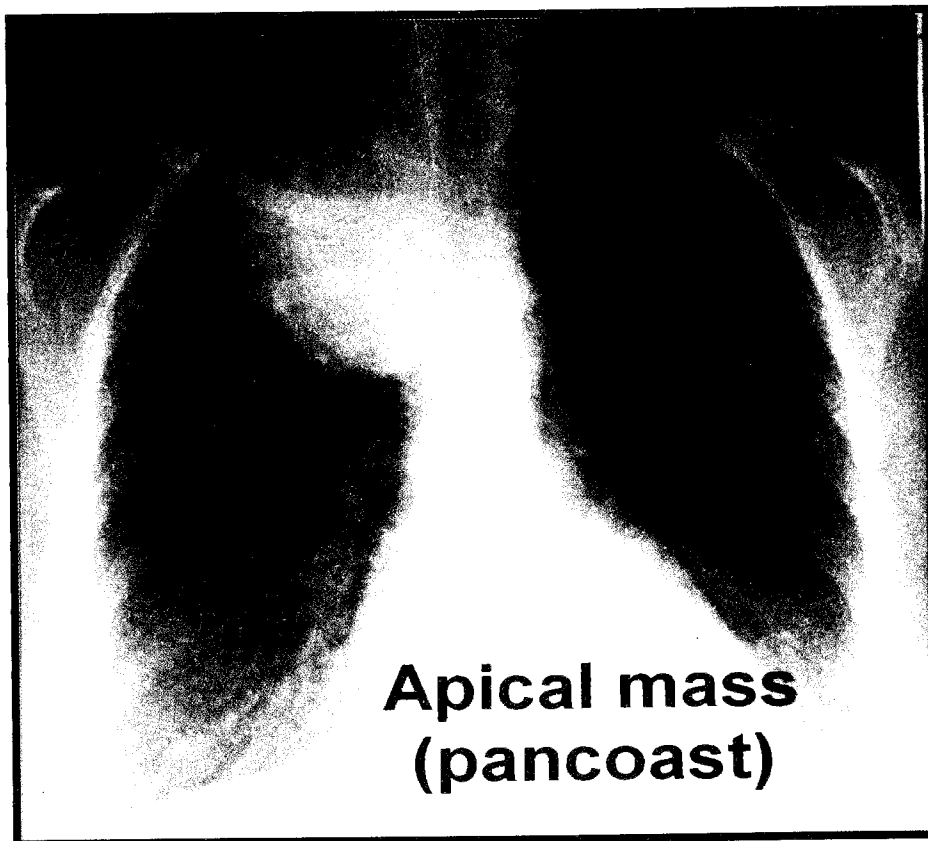
- Brain: ↑ ICT & focal neurological manifestations.

3) NON-METASTATIC PRESENTATIONS

“Paramalignant syndrome”

- CNS: Encephalomyelitis, Subacute cerebellar degeneration.
- PNS:
 - PN: Peripheral neuropathy.
 - NMJ: Myasthenia gravis, Lambert-Eaton syndrome.
 - Muscles: Secondary myopathy, Dermatomyositis.





List of famous Bronchogenic carcinoma victims

- Walt Disney
- Yul Brynner

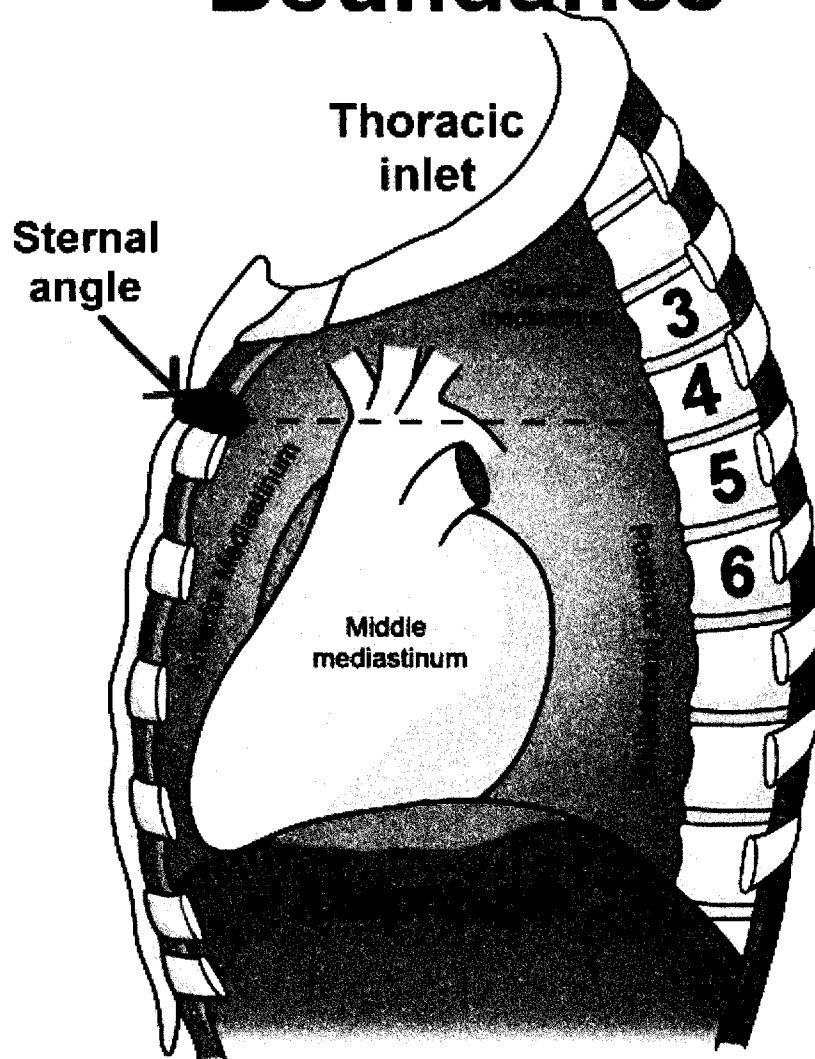
ANATOMY OF THE MEDIASTINUM

- **The mediastinum is the central part of the thorax.**
- **The mediastinum has the following boundaries:**
 - *Anteriorly: the sternum.*
 - *Posteriorly: the thoracic vertebrae.*
 - *Superiorly: the thoracic inlet.*
 - *Inferiorly: the diaphragm.*
 - *Laterally: the parietal pleura.*
- **The mediastinum is divided by an imaginary line into:**
 - Superior mediastinum.
 - Inferior mediastinum.

The line passes from the sternal angle to the lower border of the 4 th thoracic vertebra

- **The inferior mediastinum is subdivided by the pericardial sac into:**
 - Anterior mediastinum.
 - Middle mediastinum.
 - Posterior mediastinum.

Boundaries



CONTENTS OF THE MEDIASTINUM

I. Superior mediastinum:

1. Vessels:

- Arteries: Arch of the aorta & its 3 big branches.
- Veins: SVC & the 2 innominate veins.

2. Tubes:

- Upper parts of: oesophagus, trachea, thoracic duct.

3. Nerves:

- Vagus & Left RLN.
- Upper sympathetic ganglia.
- Phrenic nerves.



Autonomic nerves

II. Anterior mediastinum:

1. Thymus gland.
2. Fat.

III. Middle mediastinum:

1. Pericardial sac & its contents (heart & its big vessels).
2. Trachea & the main bronchi.
3. Phrenic nerves.

IV. Posterior mediastinum:

1. Vessels:

- Arteries: Descending aorta.
- Veins: Azygos & hemiazygos veins.

2. Tubes:

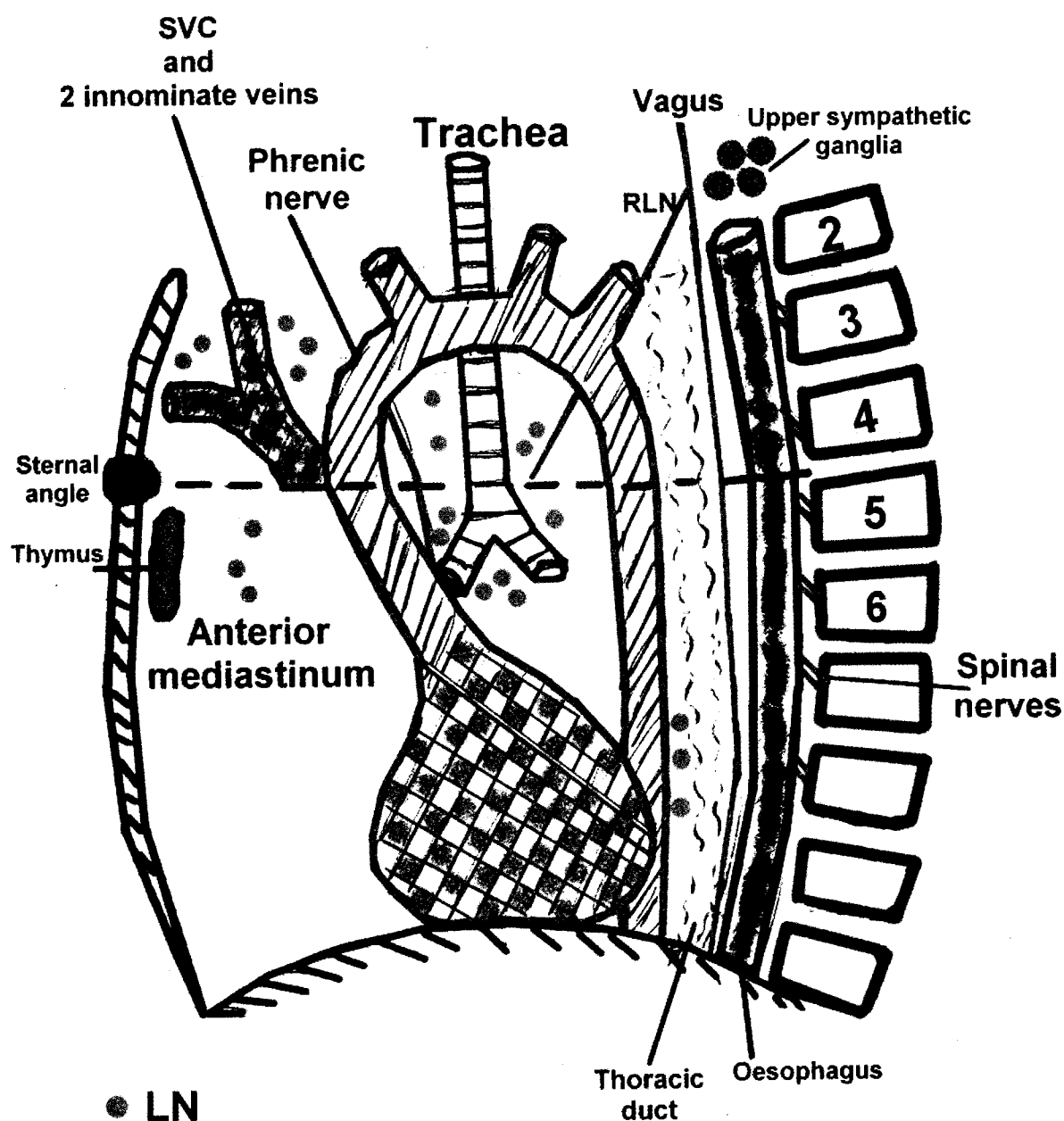
- Oesophagus.
- Thoracic duct.

3. Nerves:

- Vagus nerve.
- Spinal nerves.

NB *Lymph nodes are present in different parts of the mediastinum.*

Illustrative anatomy of the mediastinum



MEDIASTINAL SYNDROME

ETIOLOGY

I. In the Superior mediastinum:

- Aneurysm of the arch of the aorta or one of its 3 big branches.
- Tumours.
- Retrosternal goitre.
- Lymphadenopathy.

II. Anterior mediastinum:

- Thymoma.

III. Middle mediastinum:

- Aneurysm of the ascending aorta or the pulmonary artery.
- Pericardial effusion.
- Bronchial carcinoma.
- Lymphadenopathy.

IV. Posterior mediastinum:

- Aneurysm of the descending thoracic aorta.
- Oesophageal tumours.
- Hiatus hernia.
- Neurofibroma.

CLINICAL PICTURE

I. Manifestations of the cause.

II. Pressure manifestations:

1. Pressure on vessels:

A) Branches of aortic arch:

- Unequal pulse & BP in the upper limbs.

B) SVC:

- Neck veins: *congested non – pulsating.*
- Dilated veins: on the chest wall filling from above downwards.
- Oedema & cyanosis: *face, neck & upper limbs.*

2. Pressure on tubes:

A) Oesophagus:

- Dysphagia.

B) Trachea & bronchi:

- Dyspnea, stridor,
- Cough (*brassy*).
- Wheeze (*localised*).

C) Thoracic duct:

- Pericardial effusion.
- Pleural effusion.
- Peritoneal effusion (ascites).



Chylous

3. Pressure on nerves:

- | | | |
|---|---|-------------------------|
| <p>A) <u>Vagus or left RLN:</u></p> <ul style="list-style-type: none"> • Hoarseness of voice. <p>B) <u>Sympathetic chain:</u></p> <ul style="list-style-type: none"> • Horner's syndrome. | } | Autonomic nerves |
| <p>C) <u>Phrenic nerve:</u></p> <ul style="list-style-type: none"> • Diaphragmatic paralysis. | | |
| <p>D) <u>Brachial plexus:</u> (<u>lower trunk</u>)</p> <ul style="list-style-type: none"> • Pain along the medial aspect of: <i>arm, forearm, hand.</i> • Weakness & wasting of: <i>small muscles of the hand.</i> | | |
| <p>E) <u>Intercostal nerves:</u></p> <ul style="list-style-type: none"> • Intercostal neuralgia. | | |

4. Pressure on bones: (**Ribs, sternum, spine**)

- Bone pains.

INVESTIGATIONS

I. Imaging:

1. CXR:

- To detect the mediastinal mass (size & site).

2. CT & MRI chest:

- More accurate in diagnosing the mass.

3. Fluoroscopy:

- To detect the position & mobility of the diaphragm.
- To detect pulsations of an aneurysm.

4. Others:

- Echocardiography, Ba swallow, thyroid scan, lymphangiography.

II. Endoscopy:

- Bronchoscopy.
- Oesophagoscopy.
- Mediastinoscopy.

III. Exploratory thoracotomy.

TREATMENT

- **TTT of the cause.**

BLOOD

Sherif EL Hawary, MD

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BONE MARROW

- It is a spongy material in the centre of some of our bones.
- It produces cells known as stem cells.

STEM CELLS

- Immature cells that develop into 3 different types of blood cells.

BLOOD CELLS

- **Red blood cells:** carry oxygen to all cells in the body.
- **White blood cells:** fight infections and form part of our immune system.
- **Platelets:** help the blood to clot, to prevent bleeding.

NORMAL BLOOD VALUES

A) RED BLOOD CELLS

1. Red cell count:

nearly 5 millions / cmm

- In females: 4.5 – 5 millions In males: 5 – 5.5 millions.
- Increase = polycythemia Decrease = anemia.

2. Hemoglobin concentration:

nearly 15 gm %

- In females: 12 – 16 gm % In males: 13 – 17 gm %.
- Increase = polycythemia Decrease = anemia.

3. Hematocrit value OR Packed cell volume (PCV):

- It is the volume of packed red cells in 100 ml of blood.
- In females: 36 – 48 % In males: 40 – 52 %.
- Increase = polycythemia Decrease = anemia.

4. Red cell indices:

a) Mean Cell Volume (MCV):

- It is nearly 90 CM.
- In anemia: if MCV < 80 → microcytic anemia.
 if MCV 80 – 100 → normocytic anemia.
 if MCV > 100 → macrocytic anemia.

b) Mean Cell Hemoglobin Concentration (MCHC):

- It is the average hemoglobin concentration in the red cells.
- It is nearly 34 gm / dl.
- In anemia: if MCHC < 30 → hypochromic anemia.
 if MCHC 30 – 35 → normochromic anemia.
 if MCHC > 35 → hyperchromic anemia.

5. Reticulocyte count: (normally: 0.5 – 1.5 %)

- Reticulocyte: a young immature RBC newly released from the BM.
- Reticulocyte count: reflects the rate of RBC production in the BM.
- Reticulocytosis: ↑ reticulocyte count occurs in cases of over active BM:
 - *Hemolytic anemia.*
 - *Acute hemorrhage.*
 - *Anemia under ttt.*
 - *Recovery from BM suppression.*
- Reticulocytopenia: ↓ reticulocyte count occurs in cases of suppressed BM:
 - *Aplastic anemia.*

6. Red cell diameter:

- The Mean Cell Diameter (MCD) is 7.2 Microns.
- Microcytosis = less than 7.2 Microns.
- Macrocytosis = more than 7.2 Microns.
- Anisocytosis = variations in size.

7. Red cell morphology:

- Normal red cell: *Biconcave disc.*
- Abnormal red cell:
 - *Schistocytes:* *Traumatic hemolysis.*
 - *Sickle cells:* *Sickle cell anemia.*
 - *Spherocytes:* *Hereditary Spherocytosis.*
 - *Target cells:* *Thalassemia.*
 - *Teardrop RBCs:* *Idiopathic myelofibrosis.*
 - *Howell-Jolly bodies:* *Hyposplenism.*
 - *Poikilocytosis:* *Variable shapes.*

B) WHITE BLOOD CELLS

1. Total leukocytic count (TLC): 4,000 – 11,000 / cmm.
 • Increase = leukocytosis Decrease = leukopenia.

2. Differential leukocytic count:

- Neutrophils: 50 – 70 % (Staff : Segmented = 1 : 10)
- Eosinophils: 2 – 5 %.
- Basophils: 0 – 1 %.
- Lymphocytes: 20 – 40 %.
- Monocytes: 2 – 8 %.

Differential neutrophil count

- Shift to the left: ↑ Staff in overactive BM (bacterial infections).
- Shift to the right: ↑ Segmented in delayed BM (megaloblastic anemia).

Neutrophilia (> 7500 / cmm)

a) Physiological: exercise, emotional stress, pregnancy.

b) Pathological:

- **INFECTIONS** especially BACTERIAL INFECTIONS.
- **INFLAMMATIONS** e.g. collagen diseases as SLE & RA.
- **I**atrogenic: e.g. corticosteroids.
- **H**emorrhage.
- **H**emolysis.
- **T**rauma & burns.
- **T**issue injury: e.g. myocardial infarction.
- **M**alignancy: e.g. carcinoma, or blood malignancies.
- **M**etabolic: e.g. DKA, uremia.

Neutropenia (< 2000 / cmm) = Agranulocytosis = Granulocytopenia

1. **Bone marrow aplasia:** see “aplastic anemia”.
2. **Bone marrow infiltration.**
3. Immunological: autoimmune diseases.
4. Infections: Viral infections, TB, Typhoid.
5. Megaloblastic anemia.
6. Hypersplenism.

Eosinophilia

1. **Allergic** disorders: Bronchial asthma, allergic rhinitis, urticaria.
2. **Parasitic** infestations: Toxocara, Schistosoma, Filaria, Ankylostoma.
3. Skin diseases: Allergy, Psoriasis.
4. Immune: PAN, RA.
5. Malignancy: Eosinophilic leukemia, Hodgkin's disease.
6. Miscellaneous: Loeffler's syndrome, Addison's disease.

Eosinopenia

1. **A**cute infections.
2. **B**urns.
3. **C**ushing's syndrome, Corticosteroid therapy.

Basophilia

1. **M**alignancies of the blood: e.g. leukemia.
2. **M**yoedema.

Basopenia

1. Allergy.
2. Corticosteroid therapy.
3. Hyperthyroidism.

Lymphocytosis

1. Acute **VIRAL** infections: *Hepatitis, HSV, IMN, CMV.*
2. Chronic BACTERIAL infections: **TB**, Brucellosis, Syphilis.
3. Lymphomas: especially Lymphocytic lymphomas.
4. Lymphatic leukemias: acute & chronic.

Lymphopenia

1. Immunodeficiency diseases.
2. DRUGS: Immunosuppressive drugs & **Corticosteroids**.
3. Lymphomas: especially Hodgkin's disease.
4. Cushing's syndrome.
5. Malnutrition & Malabsorption.

Monocytosis

1. Infections: Brucellosis, Typhoid, TB, Syphilis, SBE, **IMN**.
2. Malignancy: Monocytic leukemias, Hodgkin's disease.
3. Miscellaneous: Collagen diseases, Sarcoidosis.

Monocytopenia

1. Aplastic anemia.
2. Infections: HIV.
3. Immune: SLE.
4. Malignancy: CLL.

C) PLATELET COUNT

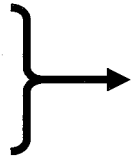
- Normally: 150,000 – 400,000 / cmm.

ANEMIA

DEFINITION

1. Reduction in:

- Red cell count
- Hemoglobin concentration
- Hematocrit value



Reduction of the O₂ carrying capacity of the blood.

THEREFORE:

2. Reduction in:

- O₂ delivery to the tissues.

COMPENSATORY MECHANISMS IN ANEMIA

Several compensatory mechanisms occur to maintain tissue oxygenation:

1. Increased O₂ delivery to the tissues:

through

- o Increased cardiac output.
- o Peripheral vasodilatation.
- o Reduced affinity of Hb to O₂.

2. Increased erythropoietin production:

to ↑ red cell production in the BM.

3. Increased plasma volume:

to maintain the total blood volume normal.

FACTORS AFFECTING THE SYMPTOMS OF ANEMIA

1. **Speed of onset:**

- Rapidly progressive anemia causes more symptoms than anemia of slow onset, because there is less time for compensatory mechanisms to occur.

2. **Severity of anemia:**

- Mild anemia may be asymptomatic.

3. **Senility:**

- Symptoms are more severe in the elderly due to:
impaired cardiovascular compensatory mechanisms in the elderly.

CLASSIFICATION

I. ETIOLOGICAL CLASSIFICATION

A) Decreased red cell production:

1. Decreased proliferation (Hypoproliferative anemia)
 - Aplastic anemia.
 - Myelophthisic anemia.
 - Anemia with organ *failure*:
 - *Renal failure*, *liver failure*, *endocrinal failure*.
2. Decreased maturation (Dyshematopoietic anemia)
 - Iron deficiency anemia.
 - Megaloblastic anemia: *B12 or folic acid deficiency*.
 - MDS.

B) Increased red cell destruction:

- Hemolytic anemias.

C) Increased red cell loss:

- Acute post – hemorrhagic anemia.

II. MORPHOLOGICAL CLASSIFICATION

A) Microcytic hypochromic anemia:

1. Iron deficiency anemia.
2. Thalassemia.
3. Sideroblastic anemia.
4. Anemia of chronic disease (ACD).

B) Normocytic normochromic anemia:

1. Aplastic anemia.
2. Myelophthisic anemia.
3. Anemia with organ *failure*.
4. Hemolytic anemia.
5. Acute post-hemorrhagic anemia.
6. Anemia of chronic disease (ACD).

C) Macrocytic anemia:

1. Megaloblastic anemia: *B12 or folic acid deficiency*.
2. Miscellaneous: *Alcohol, liver failure, reticulocytosis, Myxoedema, MDS.*

MANIFESTATIONS OF ANEMIA

I. GENERAL MANIFESTATIONS OF ANEMIA

Symptoms

1. General:

- Easy fatigue, lassitude, stunted growth *in children with chronic severe anemia*.

2. CVS:

- Palpitation, exertional dyspnea.
- Precipitation of angina, precipitation of HF (high cardiac output HF).
- Intermittent claudications in severe cases.

3. Neurological:

- Headache, dizziness, blurring of vision, syncope.
- Lack of concentration.
- Numbness & tingling: of feet & hands.

4. Genital:

- FEMALE: Menstrual irregularities, MALE: impotence.

Signs

1. Pallor: best detected in: *mm of mouth & conjunctiva, palmar creases, nail folds*.

2. Hyperdynamic circulation:

- Pulse: Tachycardia & big pulse volume.
- Heart: Accentuated heart sounds, S3, hemic murmurs.
- In severe cases: High cardiac output HF.

3. Oedema of LL: may occur due to:

- Hypoxia: which increases the capillary permeability.
- Salt & water retention.
- Anemic HF.

II. SPECIFIC MANIFESTATIONS OF ANEMIA

- These are manifestations related to the specific cause of anemia “see later”.

IRON DEFICIENCY ANEMIA

DEFINITION

- Iron deficiency is defined as: *a decreased total iron body content.*
- Iron deficiency anemia occurs when: *iron deficiency is sufficiently severe to diminish erythropoiesis and therefore cause the development of anemia.*
- It is the most common type of anemia.

ETIOLOGY

1. Decreased intake of iron:

- Infants: because iron content of milk is low.
- Elderly: and poor people.

2. Decreased absorption of iron:

- Achlorhydria: e.g. *atrophic gastritis, gastrectomy, cancer stomach.*
- Diet: $\uparrow\uparrow$ phosphate & phytate (cereals) or tannate (tea) or oxalates.
- Pica: Ingestion of unusual substances such as clay $\rightarrow \downarrow\downarrow$ iron absorption.
- MALABSORPTION SYNDROME.

3. Increased demand for iron:

- Females in child-bearing period: pregnancy & lactation.
- Growth periods: infancy & adolescence.

4. INCREASED LOSS OF IRON: (CHRONIC BLOOD LOSS)

• GIT:

- Oesophagus: varices, tumours.
- Stomach: peptic ulcer, tumours.
- Intestine: Ancylostoma infestation, Angiodysplasia, IBD, piles, tumours.

Iron deficiency in an adult male means GIT blood loss until proven otherwise

- Recurrent bleeding: epistaxis, hematuria, bleeding from wounds, menorrhagia.
- Repeated blood donation.
- Hemorrhagic blood diseases.
- Hemoglobinuria.

CLINICAL PICTURE

1. General manifestations of anemia: “ see before ”.

2. Manifestations of iron deficiency:

- **Mouth:** Angular stomatitis (Cheilosis).
- **Tongue:** Atrophy of tongue papillae.
- **Nose:** Atrophy of nasal mucosa + bad smelling discharge (**Ozena**).
- **Appetite:** Perverted appetite (**Pica**).
- **Nails:** Brittle, flattened, loss of luster + spooning (**Koilonychia**).
- **Spleen:** Mild splenomegaly (in 10 % of the cases).

3. Manifestations of specific types of iron deficiency:

A) ANCYLOSTOMA ANEMIA:

- Loss of iron: Features of iron deficiency anemia including Pica.
- Loss of proteins: Hypoalbuminemia.
- Abdominal pain, Alternating diarrhoea & constipation.
- Blood: Eosinophilia.
- Stools: Ancylostoma ova.

B) PLUMMER – VINSON SYNDROME:

(Paterson – Kelly Syndrome)

- Incidence: usually occurs in middle aged females.
- Features of iron deficiency anemia: especially,

Stomatitis, Spooning, Splenomegaly.
- DYSPHAGIA: due to oesophageal web (desquamating epithelial cells), which:
 - may obstruct the oesophagus.
 - may be complicated by: post-cricoid carcinoma.
 - may appear in Ba swallow as a: post-cricoid web.

Koilonychia “ Iron deficiency anemia ”



INVESTIGATIONS

I. For diagnosis of iron deficiency anemia:

1. CBC: “*Features of microcytic hypochromic anemia*”

RBCs:

- Decreased: Red cell count, Hemoglobin level, Hematocrit value.
- Decreased: MCV & MCHC.

WBCs:

- Usually normal.
- Eosinophilia is present in Ancylostoma infestation.

Platelets:

- Usually normal.

2. Bone marrow examination:

- Erythroid hyperplasia.
- Decreased iron stores in macrophages.

3. Evidence of iron deficiency:

- Serum iron, ferritin, transferrin saturation: decreased.
- TIBC: increased.
- FEP: increased.

II. For diagnosis of the cause:

1. Stool examination:

- For occult blood (precautions).
- For Ancylostoma ova.

2. Investigations for GIT hemorrhage:

- Endoscopies: oesophagoscopy gastroduodenoscopy, colonoscopy.
- Barium studies: Ba swallow, Ba meal, Ba enema.
- Angiography: is useful in cases of rapid bleeding.
- RADIO-ISOTOPE BLEEDING SCAN:
 - Radio-isotope scanning of the abdomen after IV injection of Technetium is useful when active bleeding is too slow to be detected by angiography.

3. Investigations for hemostatic disorders:

- See later.

4. Investigations for malabsorption syndrome:

- Refer to GIT.

5. Gastric function tests:

- To detect achlorhydria.

DIFFERENTIAL DIAGNOSIS

- Causes of: Microcytic anemia:
 1. Iron deficiency anemia.
 2. *Thalassemia.*
 3. *Sideroblastic anemia.*
 4. *Anemia of chronic disease* (ACD).

TREATMENT

I. Specific TTT

A) TTT of the underlying cause: e.g. ttt of Ancylostoma infestation.

B) Replacement therapy:

- **AIM**

1. To correct anemia: i.e. to restore the normal Hb level.
(Hb ↑ about 1 gm % weekly until normal levels are restored)
(Reticulocyte count begins to ↑ within 5 days of starting ttt)

Causes of impaired response:

- *Presence of persistent blood loss.*
- *Associated ↓ in Hb synthesis.*
- *Noncompliance to ttt.*

2. To replenish the iron stores: i.e. to provide stores of at least $1/2$ to 1 gm of iron.
(Continuous ttt for 6 months after correction of anemia will achieve this)

- **METHODS**

1. Iron – rich diet:

- Meats: beef, chicken, fish.
- Vegetables: leafy greens, legumes, peas, etc....
- Others: pasta, rice, yeast.

2. Iron preparations:

a) Oral iron:

- Preparations: *ferrous sulphate, ferrous gluconate, ferrous fumarate.*
- Dose: 300 mg tds.
- Side effects:
 - GIT irritation: *anorexia, nausea, vomiting, abdominal pain, constipation.*
 - Dark stools.

b) Parenteral iron:

- Preparations: Iron dextran (IV), or Iron sorbitol (IM).
- Dose: 100 mg / day IV or IM.
- Side effects:
 - Local: pain, inflammation, abscess formation, thrombosis.
 - General: **f**ever, **f**lushing, **h**eadache, **h**ypotension, **a**rthralgia, **a**naphylaxis.
- Indications:
 - Intolerance of oral iron.
 - Malabsorption syndrome.
 - Rapid iron loss.
 - GIT disorders that may be aggravated by oral iron:
e.g. peptic ulcer, IBD.

II. Transfusion therapy:

- Packed red cell transfusion may be needed in cases of severe anemia:
 - Hemoglobin: < 7 gm %.
 - Marked symptoms of anemia.
 - Anemic HF.

III. Symptomatic TTT:

- e.g. ttt of anemic HF.

HEMOLYTIC ANEMIA

DEFINITION

- It occurs due to: premature destruction of the RBCs → short life span of RBCs.
- It occurs when: BM activity cannot compensate for the destroyed RBCs.
- Hemolysis may be: intravascular or extravascular.

ETIOLOGY

I. CORPUSCULAR CAUSES

1. Membrane defects:

- Hereditary spherocytosis (HS).
- Paroxysmal nocturnal hemoglobinuria (PNH).

2. Hemoglobin defects: “Hemoglobinopathies”

- Thalassemias.
- Sickle cell anemia.
- Rare types: Hb C, Hb D, Hb E.

3. Enzyme defects:

- Glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency).

ALL the
corpuscular
causes
are
HEREDITARY
except:
PNH.

II. EXTRA-CORPUSCULAR CAUSES

1. Immune hemolytic anemia:

- Allo-immune: incompatible blood transfusion.
- Auto-immune: autoimmune hemolytic anemia.

2. Infections:

- Malaria, *Clostridium welchii*.

3. Physical:

- March hemoglobinuria.
- MicroAngiopathic Hemolytic Anemia: DIC, HUS, TTP.
- Prosthetic cardiac valves.

4. Chemical:

- Drugs: *Amphotericin B*.
- Toxins: *lead, copper, snake venom, RENAL FAILURE*.

5. Hypersplenism.

6. Metabolic: *Wilson's disease*.

CLINICAL PICTURE

1. **General manifestations of anemia:** “ see before ”.

2. **General manifestations of hemolytic jaundice:**

- Jaundice: MILD.
- Stools: DARK.
- Urine: NORMAL in colour: but darkens on standing.

3. **Hepatosplenomegaly:** is usually present.

4. **Gall stones & intrahepatic biliary obstruction:**

- May occur due to ↑↑ bile pigment production & will lead to: **OJ.**

5. **Leg ulcers surrounded by pigmentation:**

- May occur due to ↑↑ iron deposition under the skin.

6. **Different types of crises:**

Hemolytic crisis:

- **P**recipitating factor: Infections → hyperplasia of the RES.
- **P**allor: Marked pallor + deepening of jaundice + dark urine due to hemoglobinuria.
- **P**yrexia: Fever & rigors due to pyrogens released from the RBCs.
- **P**ain: Generalized bone pains (due to hyperactive BM) + acute abdominal pain.
- Associated with: Increased reticulocytic count.

Aplastic crisis:

- **P**recipitating factor: Viral infections → BM inhibition → no compensation for destroyed RBCs.
- **P**allor: Marked pallor, BUT: no deepening of jaundice & no dark urine.
- Associated with: Decreased reticulocytic count.

Megaloblastic crisis:

- Aggravation of anemia due to: relative folate deficiency.

Sequestrational crisis:

- Aggravation of anemia due to: pooling of the RBCs in the spleen.

Vaso-occlusive crisis:

- Painful occlusion of the blood vessels: in sickle cell anemia only.

7. **Manifestations of the cause:** e.g.

- In PNH: Iron deficiency.
- In Thalassemia: Iron overload.
- In Sickle cell anemia: Vascular occlusion.

INVESTIGATIONS

I. Diagnosis of hemolytic anemia:

1. CBC:

RBCs

- Normocytic normochromic anemia: with normal MCV & normal MCHC.
- Macrocytic anemia may occur: in megaloblastic crisis or in severe reticulocytosis.
- Microcytic anemia may occur: in case of thalassemia.
- Reticulocytic count: High, is the rule... Low in aplastic crisis.
- Blood film: may reveal characteristic red cells, e.g. sickle cells.

WBCs & Platelets

- Usually normal: BUT may ↑ due to hyperactive BM.

2. Bone marrow examination:

- Hyperplastic BM: this is the rule.
- Hypoplastic BM: in aplastic crisis.
- Megaloblastic BM: in megaloblastic crisis.

3. Measure of life span of RBCs: “using Cr – labelled red cells”

- Shortened life span of RBCs.

4. Bile pigments:

- Serum bilirubin: increased mainly the indirect.
- Stools: increased stercobilinogen.
- Urine: increased urobilinogen, absent bilirubin.

5. Serum LDH: increased.

II. Differentiating Intravascular & Extravascular hemolysis:

- Laboratory features of Intravascular hemolysis:

- **H**emoglobinuria.
- **H**emosiderinuria.
- **H**aptoglobin: *is markedly decreased in plasma.*
- **H**emopexin: *is markedly decreased in plasma.*

III. For diagnosis of the cause: e.g.

- In PNH: Flow cytometry.
- In Thalassemia: Hemoglobin electrophoresis.
- In Sickle cell anemia: Hemoglobin electrophoresis.

HEREDITARY SPHEROCYTOSIS

ETIOLOGY

- Hereditary deficiency of a protein in the MEMBRANE of the RBCs leading to:
 - RBCs become rigid (less deformable) → destruction especially in the *spleen*.
 - RBCs become more permeable to water → ↑↑ OSMOTIC FRAGILITY.
 - RBCs become small & spherical → microspherocytes.

CLINICAL PICTURE

- | | |
|-------------------------------|-------------------------------------|
| 1. GENERAL MANIFESTATIONS OF: | HEMOLYTIC ANEMIA. |
| 2. <i>Family history</i> : | <i>is usually positive.</i> |
| 3. <i>Onset</i> : | <i>is usually during childhood.</i> |

INVESTIGATIONS

- | | |
|-------------------------------|--|
| 1. GENERAL INVESTIGATIONS OF: | HEMOLYTIC ANEMIA. |
| 2. Osmotic fragility test: | ↑↑ <u>OSMOTIC FRAGILITY</u> of the RBCs. |
| 3. Blood film: | <u>microspherocytes</u> . |

TREATMENT

- | | |
|-------------------------|-------------------------------------|
| 1. Splenectomy: | prolongs the life span of the RBCs. |
| 2. Transfusion therapy: | “ see before ”. |

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

ETIOLOGY

“ UNKNOWN ”

- Acquired mutation of BM stem cells → production of cells with abnormal MEMBRANE:
- Absence of certain surface proteins (CD55 & CD59) from cell membrane of all blood cells; this will render the blood cells abnormally affected by the COMPLEMENT SYSTEM:
 - 1. RBCs: ↑↑ sensitivity to damage by complement → **Hemolytic anemia.**
 - 2. Platelets: ↑↑ platelet aggregation by complement → **Hypercoagulability & Thrombosis.**
- Associated BM hypoplasia may lead to:
 - 1. RBCs: Decreased production → aggravation of anemia.
 - 2. Platelets: Decreased production → thrombocytopenia.
 - 3. WBCs: Decreased production → leukopenia.

Pancytopenia

CLINICAL PICTURE

1. GENERAL: Manifestations of Hemolytic anemia.
2. HEMOLYSIS: **INTRAVASCULAR** with Hemoglobinuria (dark urine especially by night).
3. PAIN: Attacks of abdominal pain & back pain due to ischemia from microthrombi.
4. INFECTION: ↑↑ incidence of infection.
5. **Complications:**
 - Iron deficiency: *due to hemosiderinuria & may aggravate the anemia.*
 - Aplastic anemia: *and Acute myeloid leukemia.*
 - Thrombosis.
 - PANCYTOPENIA.

INVESTIGATIONS

1. General investigations of: **Hemolytic anemia.**
2. Investigations of: **INTRAVASCULAR HEMOLYSIS.**
3. Investigations specific for: **PNH:**
 - a) Activation of complement in the presence of RBCs → Hemolysis of RBCs, using:
 - Ham test: acidification of serum.
 - Sucrose lysis test: adding sucrose to the serum.
 - b) **Flow cytometry:** to demonstrate absent surface proteins on RBCs & WBCs:
 - CD55: DAF (Decay – Accelerating Factor).
 - CD59.

TREATMENT

1. **Symptomatic TTT:**

- Anemia: **A**ndrogens, Iron, Transfusion therapy.
- Pain: **A**nalgesics.
- Thrombosis: **A**nticoagulants.
- Infection: **A**ntibiotics.

2. **Corticosteroids:** prednisone 1 mg / Kg / day.

3. **BMT.**

HEMOGLOBINOPATHIES

- Normally: Hemoglobin is composed of:
 - Haem: iron-protoporphyrin complex.
 - Globin: protein consisting of 4 polypeptide chains.
- Normally: Hemoglobin in the adult is of 3 types:
 - Hb A (97 %): its globin is composed of: 2 alpha & 2 beta polypeptide chains.
 - Hb A₂ (1-2 %): its globin is composed of: 2 alpha & 2 delta polypeptide chains.
 - Hb F (1-2 %): its globin is composed of: 2 alpha & 2 gamma polypeptide chains, and it is the normal Hb in the fetus & diminishes after birth.
- In Hemoglobinopathies:

There are abnormalities in the structure of the globin molecule → abnormal types of Hb.

THALASSEMIAS

- Hereditary disorders of many types: the most important are alpha & beta thalassemia.

Alpha Thalassemias:

- There is ↓↓ production of alpha chains leading to production of Hb H (4 beta) & Hb Bart (4 gamma).
- There is a homozygous form (incompatible with life) & a heterozygous form (slight anemia).

Beta Thalassemias:

- There is ↓↓ production of beta chains which are replaced by:

gamma chains → production of: Hb F.

Delta chains → production of: Hb A₂.

- There are 3 types:

1. Thalassemia major: (Homozygous) = Mediterranean anemia

- Hb A is markedly reduced: while Hb F is markedly increased (> 80 – 90 %).
- It presents in adults as: **Mediterranean anemia** or **Cooley's anemia**.

2. Thalassemia minor: (Heterozygous) = Thalassemia trait

- Hb A is slightly reduced: with ↑↑ in both Hb F (5-10%) & Hb A₂ (5-10 %).
- It presents in adults by: mild microcytic hypochromic **anemia**, **splenomegaly**.
- It usually needs no ttt.

3. Thalassemia intermedia:

- Hb A is variable: it presents with moderate anemia.

Thalassemia Major Cooley's anemia Mediterranean anemia

CLINICAL PICTURE

1. GENERAL MANIFESTATIONS OF: HEMOLYTIC ANEMIA.
2. *Family history:* *is usually positive.*
3. *Onset:* *is usually during childhood.*
4. OTHER MANIFESTATIONS:
 - Iron overload: e.g. *Liver cirrhosis, skin pigmentation, diabetes, CM.*
 - Morphological features: e.g. *Mongoloid facies, stunted growth, bone deformities.*

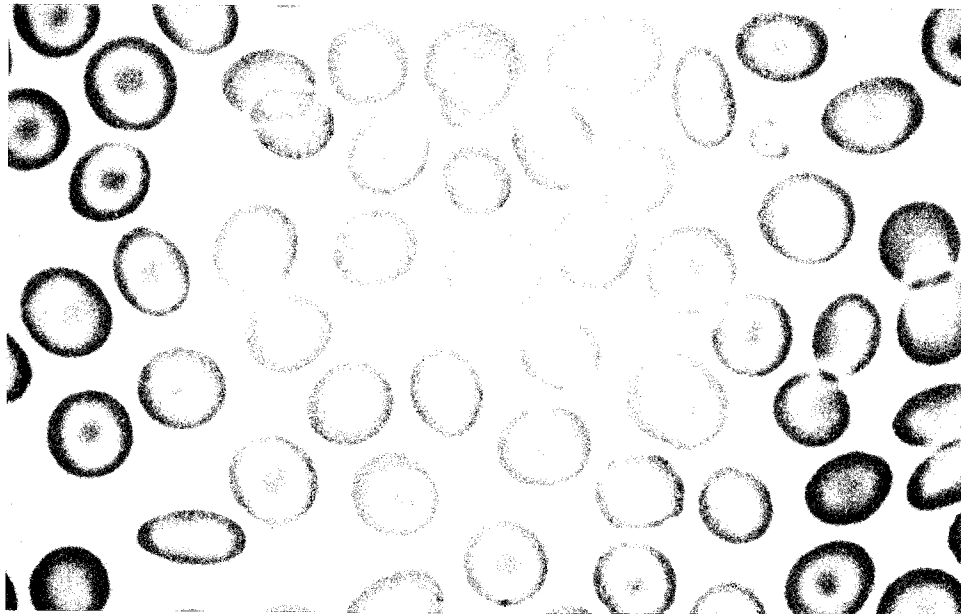
INVESTIGATIONS

1. General investigations of: Hemolytic anemia.
2. Investigations of: Microcytic hypochromic anemia.
3. Investigations specific for: THALASSEMIA:
 - Hb electrophoresis: ↑↑ Hb F (> 80 – 90 %): the most important investigation.
 - X-ray: Skull (hair-on-end appearance), Long bones (thin cortex & wide medulla).
 - Serum Iron: ↑↑ iron, ↑↑ ferritin, ↑↑ transferrin iron saturation, ↓↓ TIBC.
 - Blood film: characteristic Target cells.

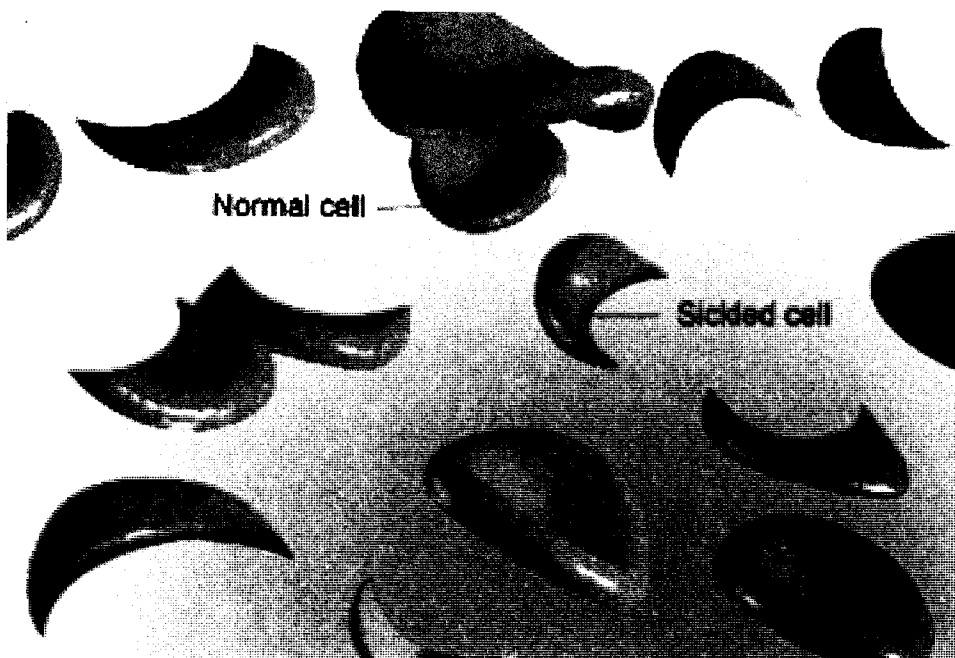
TREATMENT

1. Specific ttt:
 - a. *Repeated packed red cell transfusion:* *to keep Hb > 10 gm %.*
 - b. *Iron chelation:* *desferrioxamine by SC infusion.*
 - c. *Folic acid:* *1 mg / day.*
 - d. *Splenectomy:* *in case of hypersplenism.*
2. New lines of ttt: BMT, Gene therapy, Hydroxyurea.
3. Prevention: Prenatal diagnosis.

Beta – thalassemia with microcytes & target cells



Sickle cells



SICKLE CELL ANEMIA

ETIOLOGY

- A hereditary disorder in which there is production of an abnormal hemoglobin: **Hb S**.
- It may be homozygous (sickle cell anemia), or heterozygous (sickle cell trait).
- On exposure to HYPOXIA, Infection, or Acidosis, Hb S will form insoluble aggregates:
 - RBCs become sickle-shaped → appear on blood film.
 - RBCs become less deformable → destruction (**Hemolysis**).
 - RBCs show impaired flow → vascular **Occlusion** & tissue infarction.

CLINICAL PICTURE

- Incidence: it is common in black persons of African origin.

1. HEMOLYTIC ANEMIA.

2. VASO-OCCLUSIVE CRISES:

- **Bone** infarction: “The most common occlusion”
 - Painful crisis: attacks of severe pain in the back, chest, or extremities ± low grade fever.
 - Avascular necrosis: of the head of the femur.
- Cerebral occlusion: hemiplegia & fits.
- Pulmonary occlusion: acute pulmonary infarction, or cor pulmonale.
- Hepatic occlusion: abnormal biochemistry & pain.
- **SPLENIC** infarction: autosplenectomy & hyposplenism.
- Renal infarction: hematuria & renal failure.
- Retinal infarction: retinal detachment & blindness.
- Penile occlusion: priapism or impotence.

3. OTHER CLINICAL MANIFESTATIONS:

- Increased susceptibility to INFECTIONS: “Due to hyposplenism”
 - Pneumococcal infections.
 - Osteomyelitis caused by: Staph. aureus & Salmonella.

INVESTIGATIONS

1. General investigations of: Hemolytic anemia.
2. Investigations specific for: SICKLE CELL ANEMIA:
 - o Hb electrophoresis: detects the abnormal "Hb S" the most important investigation.
 - o Blood film: characteristic Sickle cells esp. after inducing hypoxia by adding Na bisulphate.

TREATMENT

1. Specific ttt:

- a. *Repeated packed red cell transfusion:* *to keep Hb > 10 gm %.*
- b. *Iron chelation:* *desferrioxamine by SC infusion.*
- c. *Folic acid:* *1 mg / day.*
- d. *Symptomatic ttt:* *analgesics for painful crisis.*

2. New lines of ttt: BMT, Gene therapy, Hydroxyurea.

3. Prevention: Prenatal diagnosis.

G6PD DEFICIENCY

PATHOGENESIS

- Normally:

- RBCs are protected from oxidizing stress by the HMP through producing reduced glutathione.
- RBCs contain G6PD enzyme which is essential for the HMP.

- In G6PD deficiency:

- RBCs do not contain G6PD & therefore will be unable to tolerate oxidizing stress.
- INTRAVASCULAR hemolysis of the RBCs will occur.

CLINICAL PICTURE

- Incidence: It is an X-linked disease affecting mainly males.
- The patient develops acute intravascular hemolysis when subjected to oxidizing stress:

ACUTE INTRAVASCULAR HEMOLYSIS

- Anemia.
- Hemolytic jaundice.
- Hemoglobinuria.

OXIDIZING STRESSES

- **Iatrogenic:** **A**spirin, **A**ntimalarials, **A**ntibacterials (e.g. sulphonamides).
- **Infections:** Pyogenic infections & viral hepatitis.
- **Metabolic:** DKA & CRF.
- **Meals:** Ingestion of Fava bean (FAVISM).

- FAVISM:

- **Incidence:** It is present almost only in Mediterranean populations.
- **Clinical picture:** It presents by acute hemolysis after ingestion of fava beans.
- **Pathogenesis:** It is not well understood, BUT it may be due to abnormal metabolism of beans resulting in production of oxidizing agents.

INVESTIGATIONS

1. General investigations of: Hemolytic anemia.
2. Investigations of: INTRAVASCULAR HEMOLYSIS.
3. Investigations specific for: G6PD deficiency:
 - *Estimation of G6PD.*

TREATMENT

1. Avoid oxidative stress: e.g. responsible drugs.
2. Repeated packed red cell transfusion: in severe cases.

AUTOIMMUNE HEMOLYTIC ANEMIA

A. Due to warm-reacting antibodies: “*most active at 37° C*”

ETIOLOGY

1. Idiopathic.
2. Secondary: SLE, CLL, Lymphoma.
3. Iatrogenic: Drugs (see later).

CLINICAL PICTURE

1. GENERAL MANIFESTATIONS OF: HEMOLYTIC ANEMIA.
2. SPECIFIC MANIFESTATIONS OF: the cause in secondary cases e.g. SLE.

INVESTIGATIONS

1. General investigations of: Hemolytic anemia.
2. Investigations specific for: AIHA: Positive Coomb's test.
3. Investigations for diagnosis of: the cause in secondary cases e.g. SLE.

TREATMENT

1. CORTICOSTEROIDS: Prednisone **1 mg / Kg / day** orally.
2. Immunosuppressive drugs: e.g. cyclophosphamide.
3. Transfusion therapy: may be needed in severe cases.
4. Splenectomy: may be needed in severe cases.

B. Due to cold-reacting antibodies: “most active at 4° C”

I. COLD AGGLUTININ DISEASE

- Presence of antibodies (**IgM**) that cause **Agglutination** of RBCs on exposure to cold.

ETIOLOGY

1. Idiopathic.
2. Secondary: *IMN* & *Mycoplasma pneumonia.*

CLINICAL PICTURE

1. Hemolytic anemia: *on exposure to cold.*
2. Raynaud's phenomenon: *on exposure to cold.*

INVESTIGATIONS

1. General investigations of: **Hemolytic anemia.**
2. Investigations specific for: **AIHA:** *Positive Coomb's test.*
3. Investigations for diagnosis of: the cause, *e.g. Mycoplasma pneumonia.*

TREATMENT

1. CORTICOSTEROIDS: of little benefit.
2. Immunosuppressive drugs: *e.g. cyclophosphamide.*
3. Transfusion therapy: may be needed in severe cases.
4. Splenectomy: of little benefit.
5. Avoid exposure to cold.

II. PAROXYSMAL COLD HEMOGLOBINURIA

- Presence of antibodies (**IgG**) that cause **Hemolysis** of RBCs on exposure to cold.

ETIOLOGY

1. Idiopathic.
2. Secondary: *Syphilis* & *Viral infections.*

CLINICAL PICTURE

- Hemolytic anemia: *on exposure to cold.*

INVESTIGATIONS

1. General investigations of: **Hemolytic anemia.**
2. Investigations specific for: **AIHA:** *Positive Coomb's test.*
3. Investigations for diagnosis of: the cause, *e.g. Syphilis.*

TREATMENT

- Same as: Cold agglutinin disease.

COOMB'S TEST

- It is the test used for diagnosis of autoimmune hemolytic anemia.
- It is of 2 types:
 - Direct Coomb's test:
 - *Aim:* To detect antibodies **coating** the RBCs.
 - *Method:* The patient's RBCs are mixed with Coomb's serum.
 - *Result:* Agglutination indicates a positive direct test.
 - Indirect Coomb's test:
 - *Aim:* To detect antibodies circulating **freely** in the serum.
 - *Method:* The patient's serum is incubated with compatible RBCs.
These RBCs are then washed & mixed with Coomb's serum.
 - *Result:* Agglutination indicates a positive indirect test.

DRUG INDUCED HEMOLYSIS

- Drugs may induce hemolysis through several mechanisms:

1. Direct damage: of the membrane of the RBCs.
 - e.g. Amphotericin B.
2. Oxidant drugs: in patients with G6PD deficiency.
 - e.g. **A**spirin, **A**ntimalarials, **A**ntibacterials (e.g. sulphonamides).
3. IMMUNE MECHANISMS:
 - Autoimmune reaction:
 - The drug induces the production of an antibody which destroys the RBCs.
 - e.g. alpha-methyl dopa.
 - Hapten-like reaction:
 - The drug binds to the membrane of the RBC acting as a hapten.
 - e.g. penicillin.
 - Innocent bystander reaction:
 - The drug binds to its antibody on the surface of the RBC → complement activation.
 - e.g. chlorpropamide & sulphonamides.

APLASTIC ANEMIA

DEFINITION

- A disease characterized by: *hypocellular bone marrow & peripheral blood pancytopenia.*
- Aplastic anemia: anemia due to Bone marrow failure.

ETIOLOGY

I. APLASTIC ANEMIA

“ Pancytopenia ”

a. Hereditary: Fanconi's anemia.

b. Acquired:

1. Idiopathic: The most common cause (about 50 % of the cases).
2. Iatrogenic: Dose-dependent OR Non Dose-dependent (idiosyncratic)
 - Antibiotics: e.g. **CHLORAMPHENICOL.**
 - Anti-inflammatory: e.g. NSAIDs & Gold.
 - Antiepileptics: e.g. phenytoin.
 - Antithyroid: e.g. carbimazole.
 - Antidiabetics: e.g. chlorpropamide.
 - Antineoplastics: e.g. chlorambucil.
3. Infections: **PARVOVIRUS B19, HBV, HCV, HIV, EBV.**
4. Insecticides: and chemicals as **BENZENE.**
5. Immune: SLE (rare).
6. Irradiation.
7. OTHERS: PNH, Pregnancy.

II. UNICELLULAR APLASTIA

“ Monocytopenia ”

- a. Pure red cell aplasia: e.g. associated with Thymoma, aplastic crisis of HA.
- b. Granulocytopenia: e.g. Cyclic neutropenia.
- c. Thrombocytopenia: e.g. TAR syndrome (Thrombocytopenia, Absent Radius, ASD).

CLINICAL PICTURE

- **ANEMIA** (due to ↓ RBCs).
- **INFECTIONS** (due to ↓ WBCs).
- **BLEEDING** (due to ↓ Platelets).



PANCYTOPENIA

INVESTIGATIONS

1. CBC:

“Pancytopenia”

- RBCs: NN anemia: with reticulocytopenia.
- WBCs: Leukopenia.
- PLATELETS: Thrombocytopenia.

2. Bone marrow examination:

“Aspiration & biopsy”

- Hypocellular fatty BM devoid of hematopoietic precursor cells.

3. Investigations for the cause:

e.g. markers for HBV & HCV.

DIFFERENTIAL DIAGNOSIS

1. Other causes of: PANCYTOPENIA.
2. Acute leukemia.

TREATMENT

I. Supportive TTT:

1. For anemia: packed RBCs transfusion.
2. For infections: antibiotics, G-CSF.
3. For bleeding: platelet transfusion.

II. Specific TTT:

- Withdrawal of the offending drug & ttt of the cause, **plus:**

1. BMT: It is the only curative ttt & is indicated in
 - **P**rogressive: severe aplastic anemia.
 - **P**atients less than: 45 years.
 - **P**resence of: a suitable donor.
2. Immunosuppressive therapy: “Undefined mechanisms”
 - Cyclosporin.
 - Corticosteroids: High dose.
 - Antithymocyte globulin (ATG).
3. Bone marrow stimulants:
 - Androgens.

CAUSES OF PANCYTOPENIA

1. Bone marrow failure: *Aplastic anemia.*
2. Bone marrow infiltration. *Myelophthisic anemia.*
3. Megaloblastic anemia.
4. Myelodysplastic syndromes.
5. PNH.
6. SLE.
7. Overwhelming infections.
8. Disseminated TB.
9. Hypersplenism.

CAUSES OF BM INFILTRATION

“ BM biopsy is the diagnostic procedure ”

1. Myelofibrosis:
 - Idiopathic.
2. Malignancy:
 - Blood malignancies: *Leukemias, Lymphomas.*
 - Solid malignancies: *BM metastases.*
3. Metabolic:
 - Lipid storage diseases: *Gaucher's disease.*
4. Massive infections:
 - TB *(miliary).*
 - Fungi.

CHLORAMPHENICOL & BM SUPPRESSION

1. Dose-related suppression:
 - Transient reversible aplastic anemia.
2. Non Dose-related suppression: *“ Idiosyncrasy ”*
 - Severe fatal irreversible aplastic anemia.

MEGALOBLASTIC ANEMIA

DEFINITION

- Anemia in which there is impaired DNA synthesis due to deficiency of Vitamin B₁₂ or / and folic acid:
 - Delayed division of the rapidly proliferating cells (Hematopoietic cells, GIT, Skin).
 - Production of MEGALOBLASTS in the BM & MACROCYTES in the peripheral blood.

ETIOLOGY

I. VITAMIN B₁₂ DEFICIENCY

1. Decreased intake:

- Lack of animal products.
- Vegetarian individuals.

2. Decreased absorption:

- | | |
|--|--|
| a) Deficient intrinsic factor: | <u>pernicious anemia</u> , gastrectomy, atrophic gastritis. |
| b) General Malabsorption syndrome: | <u>general causes of malabsorption including bacterial overgrowth.</u> |
| c) Specific Vitamin B ₁₂ malabsorption: | <u>Diphyllobothrium latum infestation or ileal affection.</u> |

3. Increased demand:

- Infancy.
- Pregnancy.
- Malignancy.
- Chronic hemolysis.

II. FOLIC ACID DEFICIENCY

1. Decreased intake:

- Lack of vegetables.
- Excessive alcohol intake.

2. Decreased absorption:

- | | |
|--------------------------------------|---|
| • General Malabsorption syndrome: | <u>general causes of malabsorption.</u> |
| • Specific folic acid malabsorption: | <u>Drugs: anticonvulsants, CCPs.</u> |

3. Increased demand:

- Infancy.
- Pregnancy.
- Malignancy.
- Chronic hemolysis.

4. Folic acid antagonists:

- Methotrexate.
- Co-trimoxazole.

PERNICIOUS ANEMIA

Atrophy of the gastric mucosa → decreased secretion of intrinsic factor (IF) & B₁₂ deficiency.

It is probably due to: autoimmune disease which may be genetically determined leading to:

- *Antiparietal cell antibodies that block the production of IF.*
- *Anti-IF antibodies that block the function of IF.*

It may be associated with other autoimmune diseases:

- *Autoimmune thyroiditis.*
- *Addison's disease.*

PATHOPHYSIOLOGY

- **Vitamin B₁₂ & folic acid deficiency:** Both are essential for DNA synthesis, so their deficiency will lead to deficient DNA synthesis in the dividing cells → ***Delayed division.***
- **In the Bone Marrow:** Delayed division will result in the production of MEGALOBLASTS instead of the Normoblasts. Since these Megaloblasts are abnormal cells, they will be destroyed in the bone marrow (***Intramedullary hemolysis.***)
- **In the peripheral blood:** Megaloblasts that are formed in the bone marrow will lose their nuclei and reach the peripheral blood as MACROCYTES which are large cells with increased MCV. Many of these Macrocytes are taken by the spleen and destroyed (***Extramedullary hemolysis.***)
- **ANEMIA** will result due to:
 - Delayed division of erythroid precursors.
 - Excessive hemolysis (Intramedullary & Extramedullary).
- **LEUKOPENIA & THROMBOCYTOPENIA:** similarly occur due to deficient DNA synthesis.
- **PANCYTOPENIA:** will finally occur.
- **OTHERS:**
 - GIT: Cells in the GIT show the same defect, leading to secondary atrophy of the epithelial cells of the: ***tongue, stomach, small intestine.***
 - CNS: Inability to synthesize myelin is present **ONLY** in B₁₂ deficiency and leads to neurological manifestations (**Absent in folic acid deficiency.**)

CLINICAL PICTURE

1. HEMATOLOGICAL MANIFESTATIONS

- **ANEMIA** (due to ↓ RBCs).
- **INFECTIONS** (due to ↓ WBCs).
- **BLEEDING** (due to ↓ Platelets).

PANCYTOPENIA

- HEPATOSPLENOMEGALY.

2. GIT MANIFESTATIONS

- Tongue: *Atrophic* glossitis (glazed tongue).
- Stomach: *Atrophic* gastritis (dyspepsia, anorexia, nausea, vomiting).
- Intestine: Intestinal *Atrophy* (abdominal pain, diarrhoea, malabsorption).

3. NEUROLOGICAL MANIFESTATIONS

“Only In B₁₂ Deficiency”

- Peripheral neuropathy.
- SCD of the spinal cord (refer to neurology).

4. ASSOCIATED AUTOIMMUNE DISEASES

“Only In Pernicious anemia”

- Autoimmune thyroiditis.
- Addison's disease.

INVESTIGATIONS

1. CBC:

a) RBCs:

- Features of macrocytic anemia:
 - Decreased: Red cell count, Hemoglobin level, Hematocrit value.
 - Increased: MCV (**LARGE RBCs**).
- Reticulocytosis: after giving ttt (anemia under ttt).

b) WBCs:

- Leukopenia: → with shift to the right.
- **LARGE NEUTROPHILS** (Hypersegmented).

c) Platelets:

- Thrombocytopenia.
- **LARGE PLATELETS.**

2. Bone marrow examination:

- Hypercellular megaloblastic bone marrow.
- Giant cells with abnormal morphology.

3. Blood chemistry:

- Increased: serum indirect bilirubin.
- Increased: serum iron.
- Increased: serum LDH.

4. Serum B12 & serum folic acid: “ done by radio-immunoassay ”

- Decreased.

5. Schilling test: “ Only In B12 Deficiency ”

- Unlabelled B12 is given: (1000 ug IV) to saturate the body stores.
- Radiolabelled B12 is then given: (1 ug orally).
- The patient's urine is collected for 48 hours: measure excreted Radiolabelled B12.
- If excretion is low: **B12 malabsorption is diagnosed:**
 - In *pernicious anemia*: excretion becomes normal after giving IF orally.
 - In *bacterial overgrowth*: excretion becomes normal after giving Antibiotics.
 - In *pancreatic insufficiency*: excretion becomes normal after giving Pancreatic enzymes.

6. Serology: “Only In Pernicious anemia”

- Antiparietal cell antibodies.
- Anti-IF antibodies.

7. FIGLU test: “Only In Folic Deficiency”

- Normally:

Orally given HISTIDINE is transformed into FIGLU which is converted in the presence of folic acid into glutamic acid which is excreted in urine.

- In folic acid deficiency:

Oral administration of HISTIDINE will lead to excessive excretion of FIGLU in urine (instead of glutamic acid).

8. Therapeutic tests:

- Giving small doses of Vitamin B12 or Folic acid → Reticulocytosis.

TREATMENT

1. Replacement therapy:

a) In B12 deficiency:

- Hydroxycobalamin or cyanocobalamin: 500 – 1000 ug IM / day for 2 weeks.
- Then: once / week until anemia is corrected.
- Then: once / month for life.

b) In folic acid deficiency:

- Folic acid: 1-5 mg / day orally.
- Parenteral administration may be needed: e.g. in malabsorption.
- Therapy for: 1 month is sufficient to correct the anemia.
- B12 deficiency should be excluded before giving folic acid since it may aggravate: the neurological manifestations.

2. Transfusion therapy:

- Packed red cell transfusion may be needed in cases of severe anemia:

- Hemoglobin: < 7 gm %.
- Marked symptoms of anemia.
- Anemic HF.

3. TTT of the cause & symptomatic ttt of anemia.

OTHER ANEMIAS

1. ANEMIA OF CHRONIC DISEASE (ACD).
2. ANEMIA OF LIVER DISEASE.
3. ANEMIA OF UREMIA.
4. SIDEROBLASTIC ANEMIA.
5. ANEMIA OF ENDOCRINE DISORDERS.
6. ANEMIA OF PREGNANCY.
7. ACUTE POST-HEMORRHAGIC ANEMIA.

ANEMIA OF CHRONIC DISEASE (ACD)

DEFINITION

- It is a type of anemia seen in chronic illness.
- Incidence: it is the 2nd most common type of anemia.
- Severity: it is usually mild to moderate.

ETIOLOGY

1. Chronic infection (e.g. TB).
2. Chronic inflammation (e.g. RA, SLE, IBD).
3. Malignancy (Blood, Solid).

PATHOGENESIS

1. Reduced life span of RBCs.
2. Impaired release of iron.
3. Erythropoietin (EPO) defect:
 - ↓ *production of EPO*.
 - ↓ *response to EPO in the BM*.

CLINICAL PICTURE

1. Clinical picture of the cause.
2. General clinical picture of anemia (*usually mild*).

INVESTIGATIONS

1. Investigations of the cause.
2. **Microcytic hypochromic** anemia or: NN anemia.
3. Serum iron: decreased, Serum ferritin: normal or increased.

DIFFERENTIAL DIAGNOSIS

- Causes of: Microcytic anemia:
 1. Iron deficiency anemia.
 2. *Thalassemia*.
 3. *Sideroblastic anemia*.
 4. *Anemia of chronic disease* (ACD).

TREATMENT

1. TTT of the cause.
2. Recombinant EPO.

ANEMIA OF LIVER DISEASE

- | | |
|---------------------------|--|
| 1. Liver cell failure: | Refer to “ <u>Liver notes</u> ”. |
| 2. Hepatitis: | Aplastic anemia with <u>HBV</u> , <u>HCV</u> . |
| 3. Wilson’s disease: | Hemolytic anemia. |
| 4. HCC: | ACD. |
| 5. Lipid storage disease: | Myelophthisic anemia (<u>BM infiltration</u>). |

ANEMIA OF UREMIA

- Incidence: Common.
- Severity: Usually related to the degree of uremia.

- PATHOGENESIS:

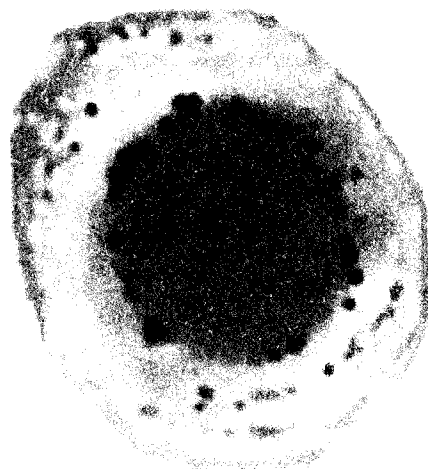
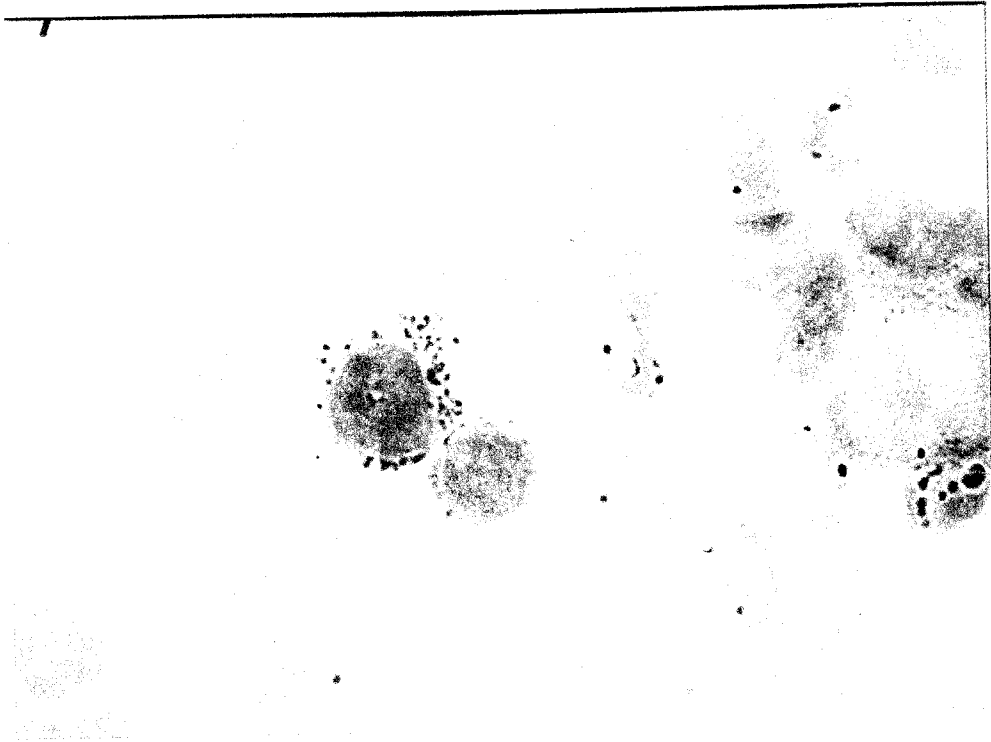
- ↓ **production of EPO.**
- ↓ iron.
- ↓ vitamins (folic acid, vitamin B₁₂).
- ↓ life span of RBCs (hemolysis).
- **HYPERPARATHYROIDISM.**

- CP: CP of uremia + general CP of anemia.
- Investigations: NN anemia + SCHISTOCYTES + impaired renal functions.
- Treatment: TTT of uremia, recombinant EPO.

SIDEROBLASTIC ANEMIA

- Etiology:
 - Hereditary.
 - Acquired: (Idiopathic: **MDS** or Secondary: RA, Malignancy, Lead).
- Pathogenesis: Inability to use iron in the formation of Hemoglobin.
- Type: Microcytic hypochromic anemia.
- Diagnosis:
 - **Ringed sideroblasts** in BM: Erythroblasts with a ring of iron granules around the nucleus.
 - **Serum iron:** increased, **Serum ferritin:** increased.
 - **FEP:** increased.

Ringed sideroblasts



ANEMIA OF ENDOCRINE DISORDERS

1. ANEMIA OF HYPOPITUITARISM:

- Normocytic: ↓ GH → ↓ tissue Oxygen needs → ↓ renal production of EPO.

2. ANEMIA OF HYPOTHYROIDISM:

- Normocytic: ↓ Thyroxin → ↓ tissue Oxygen needs → ↓ renal production of EPO.
- Macrocytic: **due to folic or B12 deficiency** or **due to associated pernicious anemia.**
- Microcytic: **due to iron deficiency secondary to malabsorption & menorrhagia in females.**

3. ANEMIA OF ADDISON'S DISEASE:

- Normocytic: ↓ Cortisol → ↓ tissue Oxygen needs → ↓ renal production of EPO.

4. ANEMIA OF GONADAL DYSFUNCTION: [In males]

- Normocytic: ↓ Androgens (Androgens normally stimulate erythropoiesis in BM).

5. ANEMIA OF PANCREATIC DYSFUNCTION:

- Anemia is common in DM: due to chronic complications of DM, e.g. CRF.

6. ANEMIA OF PARATHYROID DYSFUNCTION:

- Anemia may occur in Hyperparathyroidism: due to ↓ EPO production & BM calcification.

ANEMIA OF PREGNANCY

- Incidence: common.
- Severity: Mild to moderate, (about the 8th week of pregnancy).
- Etiology: iron deficiency, folic or B12 deficiency.

ACUTE POST-HEMORRHAGIC ANEMIA

ETIOLOGY

“Acute severe bleeding”

1. Trauma.
2. Surgery.
3. GIT ulcers.
4. Hemorrhagic blood diseases: e.g. Hemophilia, Purpura.

CLINICAL PICTURE

1. Evidence of: BLEEDING.
(Bleeding from multiple sites suggests: Hemorrhagic blood diseases).
2. General clinical picture of anemia, manifestations depend on:
 - **Rate** of bleeding.
 - **Amount** of bleeding.
 - **Time** between bleeding & presentaion.
3. There are 2 chronological CLINICAL STAGES:
 - A) FIRST STAGE: (lasts 1 – 3 days)
 - Manifestations of *hypovolemia*.
 - B) SECOND STAGE: (after 1 – 3 days)
 - Manifestations of *hypovolemia* **disappear**.
 - Manifestations of *anemia*.

INVESTIGATIONS

1. Investigations of the cause.
2. CBC:
 - RBCs: anemia (normocytic or macrocytic), reticulocytosis.
 - WBCs: leukocytosis.
 - PLATELETS: thrombocytosis (reactive).

TREATMENT

1. Treatment of the cause.
2. Symptomatic treatment: **e.g.**
 - Correction of *hypovolemia*, e.g. Blood transfusion.
 - *For anemia*.

LEUKEMIAS

DEFINITION

- Neoplasms that arise from malignant transformation of hematopoietic or lymphoid cells.
- Leukemic cells (abnormal Leukocytes) proliferate primarily in the BM, & then circulate in the peripheral blood and infiltrate other tissues.

ETIOLOGY

- The cause is UNKNOWN.
- Predisposing factors include:
 - Genetic: Incidence in **identical twins** & in **chromosomal disorders**, e.g. Down's syndrome.
 - Environmental Irradiation, Chemicals as Benzene.
 - Viral infection: Retroviruses.
 - Pre-existing disorders: PNH, MDS.

CLASSIFICATION

1. According to the clinical course:

- Acute leukemia: characterized by proliferation of **IMMATURE CELLS = BLASTS**.
- Chronic leukemia: characterized by proliferation of **MATURE CELLS = CYTES**.

2. According to the cell type:

- Lymphatic leukemia.
- Myeloid leukemia.

INCIDENCE

- Acute & chronic leukemia are nearly of equal incidence.
- Age: leukemia may affect any age, HOWEVER:
 - ALL: more common in children & young adults.
 - AML: more common in adults.
 - CLL: more common in old age.
 - CML: more common in middle & old age.

ACUTE LEUKEMIA

INCIDENCE

- ALL: more common in children & young adults.
- AML: more common in adults.

CLINICAL PICTURE

A) MANIFESTATIONS OF BM FAILURE

1. Anemia:

“ RBCs ”

- Cause: encroachment on the Red cell precursors in the BM, or due to bleeding.
- Description: *rapidly developing, progressive, severe.*

2. Bleeding:

“ Platelets ”

- Cause: encroachment on the Platelet precursors in the BM → Thrombocytopenia.
- Description: *thrombocytopenic bleeding:* “ see later ”.

3. Fever & recurrent infections:

“ WBCs ”

- Cause: non-functioning abnormal WBCs.
- Description: *in the form of:*
 - i. Common sites of infection: mouth, throat, anorectal region, UTI, lungs, skin.
 - ii. Common organisms:
 - *Gm + ve cocci:* *Staph. aureus.*
 - *Gm – ve bacilli:* *Pseudomonas.*
 - *Fungi:* *Candida.*
 - *Viruses:* *HSV.*

B) MANIFESTATIONS OF ORGAN INFILTRATION

1. Lymphadenopathy:

- Generalized LN: of small or moderate size, especially in ALL.
- Cervical LN: may be markedly enlarged & tender due to oral infection.
- Pressure manifestations: e.g. mediastinal syndrome or obstructive Jaundice.

2. Hepatosplenomegaly.

3. Generalized bone pains & STERNAL TENDERNESS.

4. Leukostasis:

- Occlusion of the microcirculation leading to **Ischemia** in different tissues.
- It affects different tissues, MAINLY: ears, eyes, brain, lungs, penis.

5. Other organs affection:

CNS

- Brain: cranial nerve palsies.
- Spinal cord: focal paraplegia.
- Meninges: meningeal irritation.

LUNGS

- Hemoptysis.

KIDNEYS

- Hematuria, ARF.

BONES

- Bony pains & pathological fractures.

JOINTS

- Joint effusion & arthritis.

GIT

- Ulcers & hemorrhage.

GUMS

- Ulcers & hypertrophy, especially in: Monoblastic leukemia.

SKIN

- Rash & nodules.

SEROUS MEMBRANES

- Pericardial effusion, pleural effusion, ascites.

TESTIS

- Testicular swelling, especially in: ALL.

C) METABOLIC MANIFESTATIONS

- Hyperuricemia: may lead to urate nephropathy & gouty arthritis.
- Hypokalemia: may occur due to renal tubular defect.
- Hyponatremia: may occur due to “SIADH”.

INVESTIGATIONS

1. CBC:

- WBCs: “ Leukocytosis ”

1. TLC: Increased, may reach 100,000 / cmm.
2. Cells: BLASTS are predominant (myeloblasts or lymphoblasts).

3. SPECIFIC TYPES:

- i. Subleukemic leukemia: TLC is normal with presence of: **BLASTS**.
- ii. Aleukemic leukemia: TLC is normal with: **no BLASTS**,
in this case the diagnosis depends on BM examination.

	Myeloblasts	Lymphoblasts
Cell morphology		
Cytochemistry	Myeloperoxidase + ve	PAS + ve

- RBCs:

- Normocytic normochromic anemia.

- PLATELETS:

- *Thrombocytosis,* or *Thrombocytopenia.*

2. Bone marrow examination:

- Hypercellular: infiltrated with sheets of BLASTS that replace the normal BM cells.
- BLASTS: more than 30 % & may reach up to 100 % of BM cells.
- BLASTS: myeloblasts or lymphoblasts.

3. Metabolic abnormalities:

- Serum uric acid: increased.
- Serum LDH: increased.
- Serum vitamin B12: increased
- Serum potassium: *may be decreased.*
- Serum sodium: *may be decreased.*

DIFFERENTIAL DIAGNOSIS

1. CLINICALLY: Acute leukemia should be differentiated from:

- APLASTIC ANEMIA.
- *Fever with LN.*
- *Fever with sore throat.*
- Rheumatic fever.
- Miliary TB.

2. LEUKEMOID REACTION:

- It is defined as marked leukocytosis (25,000 / cmm) & may be associated with: IMMATURE LEUKOCYTES.
- Myeloid leukemoid reaction:
 - BM infiltration: (myelophthisic anemia).
 - BM stimulation: severe Hemolysis, severe Hemorrhage, severe Hypoxia.
- Lymphatic leukemoid reaction:
 - Hepatitis.
 - HSV, IMN, CMV.
 - TB, Brucellosis, Syphilis.

TREATMENT

I. Supportive ttt:

- | | |
|-----------------------|---|
| 1. For anemia: | packed red cell transfusion. |
| 2. For bleeding: | platelets transfusion. |
| 3. For infections: | isolation + <u>antibiotics</u> , <u>antifungal</u> , <u>antiviral drugs</u> . |
| 4. For hyperuricemia: | Allopurinol. |
| 5. For leukostasis: | Leukapheresis. |

II. Specific ttt:

1. Chemotherapy with or without radiotherapy:

A) ALL:

1. Induction of remission: Vincristine, prednisone: for 4 weeks.
2. CNS prophylaxis: Intrathecal methotrexate.
3. Consolidation: Vincristine, prednisone.
4. Maintenance: Vincristine, prednisone, + methotrexate + 6 MP.

B) AML:

1. Induction of remission: Cytosine arabinoside, Daunorubicin: for 7 days.
2. Maintenance: Cytosine arabinoside, Daunorubicin: for 1 year.

2. BMT:

It is indicated in:

- **P**rogressive: & refractory cases.
- **P**atients less than: 45 years.
- **P**resence of: a suitable donor.

CHRONIC MYELOID LEUKEMIA

CLINICAL PICTURE



A) MANIFESTATIONS OF ORGAN INFILTRATION

1. SPLENOMEGALY:

Pain:

- Dragging pain in the left hypochondrium: due to splenomegaly.
- Stitching pain in the left hypochondrium: due to perisplenitis, resulting from splenic infarction (due to leukostasis or thrombosis).

Spleen:

- HUGE size: usually occurs.
- SPLENIC RUB: is usually heard + multiple notches due to infarctions.

2. Hepatomegaly:

- The liver may also be enlarged, or even huge, with rounded border.

3. Lymphadenopathy:

- Slight LN enlargement occurs rarely.

4. Generalized bone pains & STERNAL TENDERNESS.

5. Leukostasis:

- Occlusion of the microcirculation leading to Ischemia in different tissues.
- It affects different tissues, MAINLY: ears, eyes, brain, lungs, penis.

6. Other organs affection:

- Leukemic infiltrations of other organs are RARE.

B) MANIFESTATIONS OF BM FAILURE

1. Anemia.
2. Bleeding.
3. Fever & recurrent infections.

C) METABOLIC MANIFESTATIONS

- Hyperuricemia: may lead to urate nephropathy & gouty arthritis.

D) BLAST CRISIS

- 70 % of the patients will eventually develop transformation into AML.

INVESTIGATIONS

1. CBC:

- WBCs: “Leukocytosis”

1. TLC: Increased, may reach 100,000 - 1,000,000 / cmm.
2. Cells: MYELOCYTES are predominant with few MYELOBLASTS.
MYELOBLASTS increase markedly in Blast crisis.
3. LAP: Decreased.

- RBCs:

- Normocytic normochromic anemia.

- PLATELETS:

- *Thrombocytosis,* or *Thrombocytopenia.*

2. Bone marrow examination:

- Hypercellular & full of MYELOCYTES, with few MYELOBLASTS.
- MYELOBLASTS increase markedly in Blast crisis.

BLAST CRISIS: 30 % or more MYELOBLASTS are present in the BM and / or peripheral blood.

3. Metabolic abnormalities:

- Serum uric acid: increased.
- Serum LDH: increased.
- Serum vitamin B12: increased.

4. The Philadelphia chromosome:

- Acquired chromosomal abnormality: present in 90 % of patients with CML.
- It results from: translocation of a part of the long arm of chromosome number 22 to the long arm of chromosome number 9.

DIFFERENTIAL DIAGNOSIS

1. CLINICALLY: CML should be differentiated from:

- CLL.
- Causes of: HUGE SPLENOMEGALY (see later).
- Causes of: Myeloproliferative disorders:
 - CML.
 - PRV.
 - Essential thrombocythemia.
 - Idiopathic myelofibrosis.



2. LABORATORY: LEUKEMOID REACTION: “see before”

- It is defined as marked leukocytosis (25,000 / cmm) & may be associated with: immature leukocytes.
- It is mainly differentiated from CML by:

	Leukomoid reaction	CML
<i>Splenomegaly</i>	Rare	Common
<i>LAP</i>	High	Low
<i>Philadelphia chromosome</i>	Absent	Present in 90 % of cases

TREATMENT

I. Supportive ttt:

1. For anemia: packed red cell transfusion.
2. For bleeding: platelets transfusion.
3. For infections: isolation + antibiotics, antifungal, antiviral drugs.
4. For hyperuricemia: Allopurinol.
5. For leukostasis: Leukapheresis.

II. Specific ttt:

1. Chemotherapy:

Busulfan: (Myeleran) 4 – 8 mg / day orally

- It should be stopped when TLC is reduced below 25,000 / cmm.
- Side effects: *BM failure, pulmonary fibrosis, vomiting & diarrhoea.*

Hydroxyurea: 1 – 6 **gm** / day orally

- It has less side effects & better results than Busulfan.

2. Interferon – alpha.

3. BMT: It is the only curative ttt & is indicated in:

- **P**rogressive: & refractory cases.
- **P**atients less than: 30 years.
- **P**resence of: a suitable donor.

4. TTT of Blast crisis:

- TTT is similar to AML but with a poor response.

CHRONIC LYMPHATIC LEUKEMIA

- It is the most common form of leukemia in adults especially in: old age.
- CLL is closely related to (and most consider it the same as):
SLL, small lymphocytic lymphoma a type of non-Hodgkin's lymphoma.

CLINICAL PICTURE

1. **Asymptomatic:** occurs in 25 % of the cases.
2. **LYMPHADENOPATHY:** “ The most important manifestation ”
 - Generalized LN: of moderate size, firm, discrete, NOT TENDER.
 - Pressure manifestations: e.g. mediastinal syndrome or obstructive Jaundice.
3. **Hepatosplenomegaly.**
4. **Leukemic infiltrations of other organs may occur.**
5. **Anemia:** due to:
 - Autoimmune hemolytic anemia (positive Coomb's test).
 - BM infiltration.
 - Hypersplenism.
 - Bleeding.
6. **Bleeding:** due to thrombocytopenia, due to:
 - Autoimmune thrombocytopenia.
 - BM infiltration.
 - Hypersplenism.
7. **Fever & recurrent infections.**

INVESTIGATIONS

1. CBC:

- WBCs: “ **Leukocytosis** ” MAINLY “ **Lymphocytosis** ”
 - TLC: Increased, may reach 100,000 - 1,000,000 / cmm.
 - Cells: SMALL LYMPHOCYTES are predominant.
- RBCs:
 - Normocytic normochromic anemia.
 - Hemolytic anemia: *with positive Coomb's test.*
- PLATELETS:
 - *Thrombocytosis,* or *Thrombocytopenia.*

2. Bone marrow examination:

- Hypercellular & full of: SMALL LYMPHOCYTES (> 30 %).

3. Lymph node biopsy:

- Infiltration with: SMALL LYMPHOCYTES.

4. Metabolic abnormalities:

- Serum uric acid: increased.
- Serum LDH: increased.

DIFFERENTIAL DIAGNOSIS

- CML.
- Causes of: Lymphocytosis.
- Causes of: Generalized LN enlargement: especially Lymphoma.

TREATMENT

I. Supportive ttt:

1. For anemia: packed red cell transfusion.
2. For bleeding: platelets transfusion.
3. For infections: isolation + antibiotics, antifungal, antiviral drugs.
4. For hyperuricemia: Allopurinol.

II. Specific ttt:

1. Chemotherapy:

- Chlorambucil: (leukeran) 0.1 mg / Kg / day orally.
- Prednisone: 1 mg / Kg / day orally.

2. Radiotherapy:

- Irradiation of LN & spleen may be needed.

POLYCYTHEMIA

DEFINITION

- Increase in red cell mass: > 36 ml / Kg in males & > 32 ml / Kg in females.

ETIOLOGY

A) Secondary polycythemia:

1. Chronic hypoxia (e.g. COPD & other causes of chronic central cyanosis).
2. Cushing's syndrome & prolonged corticosteroid therapy.
3. Renal disease (e.g. hypernephroma & hydronephrosis) → ↑ EPO.
4. Paramalignant syndrome (e.g. HCC).
5. Dehydration → hemoconcentration (false polycythemia).

B) Polycythemia Rubra Vera:

“PRV”



- A myeloproliferative disorder (blood malignancy) characterized by:

“Excessive proliferation of”

<i>ERYTHROIDS in BM</i>	→	↑ <i>RBCs</i>	<i>in the peripheral blood.</i>
<i>MYELOIDS in BM</i>	→	↑ <i>WBCs</i>	<i>in the peripheral blood.</i>
<i>MEGAKARYOCYTES in BM</i>	→	↑ <i>Platelets</i>	<i>in the peripheral blood.</i>

CLINICAL PICTURE

1. Plethoric appearance.

2. Symptoms due to Hyperviscosity:

- Neurological: *headache, dizziness, tinnitus, blurring of vision, parasthesias.*
- CVS: *dyspnea, palpitation, precipitation of angina.*
- EYE: *conjunctival suffusion, retinal venous engorgement.*

3. In PRV:

- MANIFESTATIONS:

- Hepatomegaly.
- SPLENOMEGALY: *HUGE size.*
- Peptic ulcer: *due to associated increase in Histamine level.*
- Pruritus.

- COMPLICATIONS:

- Vascular thrombosis: *e.g. Stroke.*
- Bleeding tendency. *e.g. Stroke.*
- Hypertension.
- Hyperuricemia.

4. In secondary polycythemia:

- Features of the cause.

INVESTIGATIONS

1. CBC:

- RBCs:
 - Increased number (above 6 million / cmm).
- WBCs:
 - Increased number (above 12,000 / cmm).
- PLATELETS:
 - Increased number (above 400,000 / cmm).



In PRV ONLY

2. Bone marrow examination:

- HYPERCELLULARITY of ALL bone marrow elements.

In PRV ONLY

3. **ESR:** Low.

4. **Red cell mass:**

- Increased: > 36 ml / Kg in males & > 32 ml / Kg in females.

5. **Tests to differentiate between Secondary polycythemia & PRV:**

A. ARTERIAL BLOOD GASES:

- In secondary polycythemia: Decreased oxygen saturation.
- In PRV: Normal oxygen saturation.

B. SERUM EPO:

- In secondary polycythemia: Increased.
- In PRV: Normal or low.

6. **Others:**

- Serum uric acid: increased.
- Serum LAP: increased.
- Serum vitamin B12: increased.

DIAGNOSIS OF PRV

A

- A1: Increased Red cell mass: > 36 ml / Kg in ♂ & > 32 ml / Kg in ♀.
 A2: Normal oxygen saturation.
 A3: Splenomegaly.

B

- B1: Increased Platelets: > 400,000 / cmm.
 B2: Increased WBCs: > 12,000 / cmm.
 B3: Increased LAP.
 B4: Increased serum vitamin B12.

- DIAGNOSIS is established if the following combinations are present:

- A1 + A2 + A3, or:
- A1 + A2 + any 2 from category B.

TREATMENT

A) PRV

1. Repeated venesection: *to keep the Hematocrit value in the range of 45 %.*
2. Chemotherapy:
 - Hydroxyurea: is the best.
 - Radioactive phosphorus, Busulphan: may be used.
3. TTT of complications.

B) Secondary polycythemia:

1. Repeated venesection: *to keep the Hematocrit value in the range of 45 %.*
2. TTT of the cause.

IDIOPATHIC MYELOFIBROSIS

DEFINITION

- Progressive generalized fibrosis of the BM, associated with:
- Haemopoiesis in the *liver & spleen* (known as: Myeloid Metaplasia).



ETIOLOGY

UNKNOWN

EARLY

Idiopathic abnormal change in the stem cell in the BM leading to:

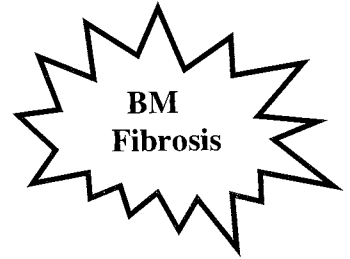
- Decreased production of: RBCs.
- Increased production of: WBCs.
- Increased production of: abnormal MEGAKARYOCYTES.
- Abnormal Megakaryocytes secrete: GROWTH FACTORS.
- Growth factors stimulate: FIBROBLASTS to produce fibrosis of BM.

LATE

Excessive BM fibrosis will ↓↓ the ability of the BM to make blood cells:
→ Decreased all blood cells → PANCYTOPENIA.

CLINICAL PICTURE

- | | |
|-------------------------|-----------------------------------|
| 1. Decreased RBCs: | General manifestations of anemia. |
| 2. Decreased WBCs: | Fever & recurrent infections. |
| 3. Decreased platelets: | Purpura & bleeding tendency. |
| 4. SPLENOMEGALY: | HUGE size. |
| 5. Hepatomegaly: | Mild. |



INVESTIGATIONS

1. CBC:

"Pancytopenia"

- RBCs: Normocytic normochromic anemia: with teardrop RBCs.
- WBCs: Early Leukocytosis, Late Leukopenia.
- PLATELETS: Early Thrombocytosis, Late Thrombocytopenia.

2. Bone marrow examination:

"Aspiration & biopsy"

- Aspiration: BM specimen cannot be obtained.
- Biopsy: Fibrotic BM.

DIFFERENTIAL DIAGNOSIS

1. Other causes of: PANCYTOPENIA.
2. Other causes of: HUGE SPLENOMEGALY.
3. Other causes of: Myeloproliferative disorders.

TREATMENT

I. Supportive TTT:

- For deficient blood cells: Repeated Blood transfusion.
- For splenomegaly: Splenectomy or radiotherapy (spleen shrinkage).

II. Specific TTT:

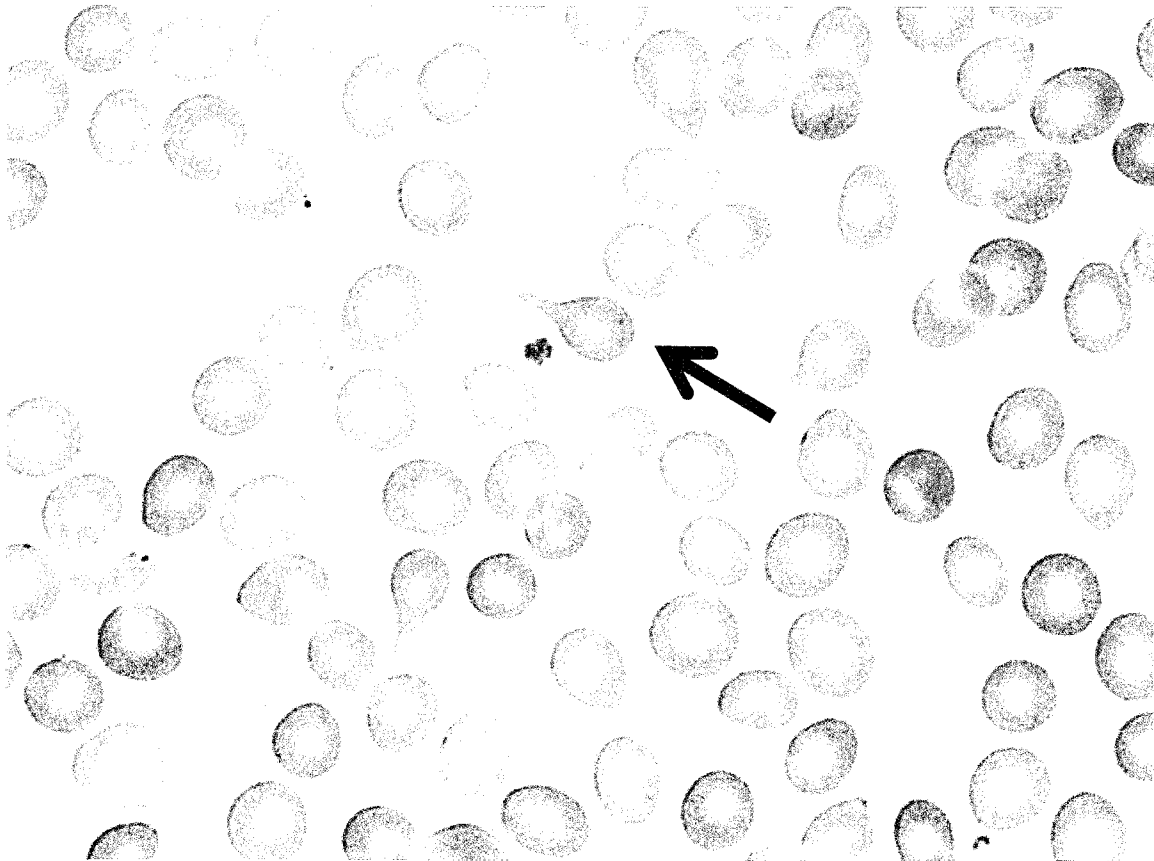
1. Chemotherapy:

- Hydroxyurea.

2. Stem cell transplantation:

- It is the only hope for cure.

Teardrop RBCs in Idiopathic myelofibrosis



NORMAL HEMOSTASIS

Three mechanisms are involved to prevent bleeding from injured blood vessels:

1. VESSEL WALL:

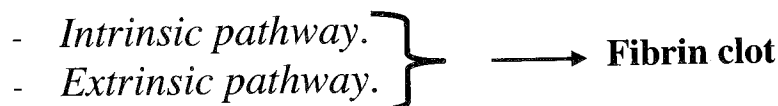
- Vasoconstriction of injured vessel is IMMEDIATE & involves 2 events:
- Reflex vasoconstriction of adjacent arteries & arterioles:
this slows the blood flow to the area of injury.
- Slow blood flow to the area of injury: *will allow contact activation of platelets & coagulation factors.*

2. PLATELET REACTION: "PRIMARY HEMOSTASIS"

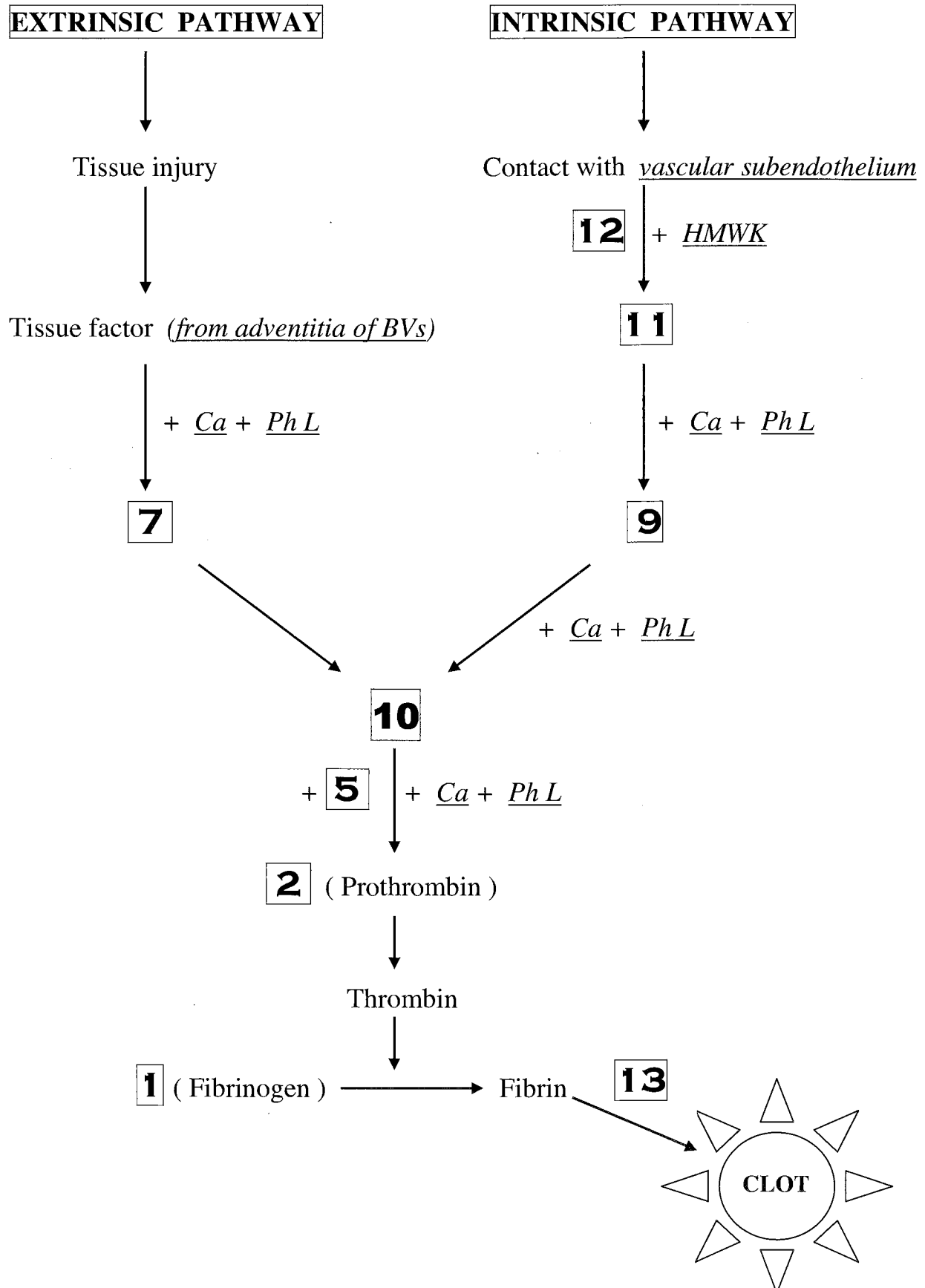
- It occurs within SECONDS of injury & involves 3 events:
- Platelet adhesion: *to the exposed subendothelium is the initial response.*
- Platelet aggregation: *then occurs to form the obstructing platelet plug.*
- Granule release: *accelerates coagulation process by providing Ph L. accelerates clot retraction / compaction.*

3. COAGULATION SYSTEM: "SECONDARY HEMOSTASIS"

- It requires several MINUTES for completion & involves 2 pathways:



COAGULATION PATHWAYS



GENERAL TESTS FOR HEMOSTASIS

1. BLEEDING TIME

BT

(2 – 7 minutes)

- Normally: It measures platelet plug formation.
- Prolonged: Diseases affecting the PLATELETS:
 - o *Thrombocytopenia* " Decreased platelets "
 - o *Thrombocytopathy* " Diseased platelets "

2. COAGULATION TIME

CT

(5 – 10 minutes)

- Normally: It measures coagulation function (coagulation factors).
- Prolonged: All types of COAGULATION disorders.

3. PROTHROMBIN TIME

PT

(12 – 14 seconds)

- Normally: It measures the function of the extrinsic & common pathways.
It is measured by: adding **Tissue factor** + Ca + Ph L to the plasma and measuring the time to clot formation.
- Prolonged: Diseases of both the extrinsic & common pathways:
 - o *Diminished factors*: **7, 10, 5, 2, 1.**
 - o *Liver cell failure.*
 - o *Vitamin K deficiency* (OJ, oral anticoag, malabsorption syndrome).

4. ACTIVATED PARTIAL THROMBOPLASTIN TIME APTT (30 – 40 seconds)

- Normally: It measures the function of the intrinsic & common pathways.
It is measured by: adding **Kaolin** + Ca + Ph L to the plasma and measuring the time to clot formation.
- Prolonged: Diseases of both the intrinsic & common pathways:
 - o *Diminished factors*: **12, 11, 9, 8, 10, 5, 2, 1.**

5. THROMBIN TIME

TT

(9 – 11 seconds)

- Normally: It measures the ability to convert Fibrinogen to Fibrin.
It is measured by: adding **Thrombin** to the plasma and measuring the time to clot formation.
- Prolonged: Diseases affecting FIBRINOGEN:
 - o *Fibrinogen deficiency* (*afibrinogenemia*).
 - o *Fibrinogen dysfunction* (*dysfibrinogenemia*).
 - o *Fibrinogen inhibitors* (*patients on heparin*).
 - o *DIC.*

HEMOSTATIC DISORDERS

TYPES

I. PURPURA

- Bleeding tendency due to defects in PLATELETS or in VESSEL WALL.

II. COAGULOPATHY

- Bleeding tendency due to defects in COAGULATION FACTORS.

I. PURPURA

A) PLATELET DEFECT

1. Thrombocytopenia:

“ Decreased platelets ”

a) Decreased platelet production:

- **B**one marrow failure.
- **B**one marrow infiltration.
- **M**egaloblastic anemia.
- **M**yelodysplastic syndromes.
- *PAROXYSMAL NOCTURNAL HEMOGLOBINURIA*.

b) Increased platelet destruction:

- Autoimmune: **Primary** (*ITP*), **Secondary** (*SLE*, *CLL*, *Lymphoma*, *drugs* as α -meth-d).
- Acute infections.
- Hypersplenism.
- DIC, TTP, HUS.

2. Thrombocytopathy:

“ Diseased platelets ”

a) Hereditary:

e.g. *Glanzmann's disease*.

b) Acquired:

- Uremia.
- Multiple myeloma.
- Thrombocytosis.
- Antiplatelet drugs: *aspirin*, *dipyridamole*, *ticlopidine*, *clopidogrel*.
- Autoimmune: *SLE*.

B) VESSEL WALL DEFECT

(Vascular Purpura)

- **I**mmune: Vasculitis e.g. SLE, PAN, Henoch-Schonlein purpura.
- **I**nfection: SBE, meningococemia.
- **I**atrogenic: Salicylates, Sulphonamides, Penicillins, Corticosteroids.
- **I**diopathic: Purpura simplex.
- **S**curvy.
- **S**enile purpura.
- **C**ushing's syndrome.
- **C**ongenital: Ehlers-Danlos syndrome.

II. COAGULOPATHY**A) HEREDITARY**

- Hemophilia.
- Fibrinogen defect: Afibrinogenemia, Dysfibrinogenemia.

B) ACQUIRED

- Liver **failure**.
- Renal **failure**.
- Deficiency of vitamin K.
- DIC.
- Drugs: Heparin, oral anticoagulants, fibrinolytic agents.

CLINICAL PICTURE**I. BLEEDING:****A) In Purpura:****1. Site of bleeding:**

- Orificial: epistaxis, melen, **Hematochezia**, **Hematemesis**, **Hemoptysis**, **Hematuria**.
- Cutaneous: petichae, ecchymosis, excessive bleeding from wounds, + ve Hess test.
- MM: oral, gingival, conjunctival.
- Internal: intracranial hge, retinal hge, cavitary hge (serous membranes).

2. Mechanism of bleeding:

- Bleeding: spontaneous or post-traumatic.

3. Character of bleeding:

- Bleeding: immediate.

B) In Coagulopathy:

1. Site of bleeding:

- Orifical: *epistaxis, melena, **Hematochezia**, **Hematemesis**, **Hemoptysis**, **Hematuria**.*
- Cutaneous: *petichae, ecchymosis, excessive bleeding from wounds, - ve **Hess test**.*
- MM: *oral, gingival, conjunctival.*
- Internal: *hemarthrosis, muscle hematoma, others like in purpura.*

2. Mechanism of bleeding:

- Bleeding: *spontaneous or post-traumatic.*

3. Character of bleeding:

- Bleeding: *delayed.*

II. ANEMIA:

- Acute & chronic post-hemorrhagic anemia may occur.

III. SHOCK:

- Severe hemorrhage may lead to: *hypovolemia & shock.*

IV. MANIFESTATIONS OF THE CAUSE.

Hess test (capillary fragility test)

Method: A circle 5 cm in diameter is marked on the antecubital fossa. The Sphygmomanometer is inflated to midway between SBP & DBP for 5 minutes. Count the number of petichae within the circle.

Result: Positive test means the presence of more than 10 petichae.

Value: It is POSITIVE in all cases of purpura

INVESTIGATIONS

A) Screening investigations:

- GENERAL TESTS FOR HEMOSTASIS.

B) Specific investigations:

1. PLATELETS:

- Platelet count: Decreased in thrombocytopenia.
- Platelet function tests: to estimate platelet aggregation.

2. CBC:

- May detect the cause of thrombocytopenia (e.g. leukemia).

3. BM examination:

- May detect the cause of thrombocytopenia (e.g. aplastic anemia).

4. ASSAY:

- Coagulation factors assay, FDPs assay.

IDIOPATHIC THROMBOCYTOPENIC PURPURA

ETIOLOGY

- Autoimmune disease in which **antiplatelet antibodies** (usually IgG) are present.
- These autoantibodies directed against glycoprotein IIb / IIIa of the platelets, will sensitize the platelets resulting in their premature removal from the circulation by macrophages of the **RES**, especially the **SPLEEN**.
- The life span of platelets is reduced to few hours (*normally: 7 days*).

CLINICAL TYPES

“ 2 types ”

I. ACUTE ITP

Age: children.

Sex: equal.

Onset: acute.

Course:

- 90 %: **resolve** spontaneously within 2 weeks to 6 months.
- 10 %: develop **chronic** ITP (lasting > 6 months).

CP: see before.

Investigations:

- Platelets: markedly ↓↓ (usually below 20,000 / cmm).
- BT: prolonged.
- CT: normal.
- PT: normal.
- APTT: normal.
- TT: normal.
- BM examination: increased number & size of megakaryocytes with:
“ defective budding ”.
- Antiplatelet antibodies: Antiglycoprotein IIb / IIIa antibodies are detected.

Treatment:

1. General measures:

- Avoid: *trauma, invasive procedures, antiplatelets.*

2. Specific measures:

- Prednisone: 1 mg / Kg / day.
- Platelet transfusion: in cases of severe hemorrhage.
- IV gamma globulins.

II. CHRONIC ITP

Age: young adults & middle age.

Sex: more common in females.

Onset: gradual.

Course:

- Prolonged for: *months* or *years* with remissions & exacerbations.

CP: see before.

Investigations:

- Platelets: moderately ↓↓ (usually 20,000 – 100,00 / cmm).
- BT: prolonged.
- CT: normal.

- PT: normal.
- APTT: normal.
- TT normal.

- BM examination: increased number & size of megakaryocytes with:
 “defective budding”.

- Antiplatelet antibodies: Antiglycoprotein IIb / IIIa antibodies are detected.

Treatment:

1. General measures:

- Avoid: *trauma, invasive procedures, antiplatelets.*

2. Specific measures:

- Prednisone: 1 mg / Kg / day.
- If no response: *splenectomy.*
- If no response:
 - Immunosuppressives: Cyclophosphamide or Cyclosporin.
 - Danazol.
- Platelet transfusion: in cases of severe hemorrhage.
- IV gamma globulins.

HEMOPHILIA

ETIOLOGY

- It is a hereditary deficiency of AHG (factor VIII) transmitted as X-linked from: healthy female carriers to their male offsprings.

CLINICAL PICTURE

<u>Age:</u>	since birth.
<u>Sex:</u>	males.
<u>Family history:</u>	positive.
<u>CP:</u>	see before.

INVESTIGATIONS

- | | |
|--------------------|---------------------|
| 1. CT: | prolonged. |
| 2. APTT: | prolonged. |
| 3. TT: | normal. |
| 4. PT: | normal. |
| 5. BT: | normal. |
| 6. Platelet count: | normal. |
| 7. Serum AHG: | markedly decreased. |

TREATMENT

- General measures:** avoid: *trauma, invasive procedures, antiplatelets.*
- Specific measures:** “ttt of bleeding episodes”
 - Factor VIII replacement: *factor VIII concentrates, fresh frozen plasma.*
 - Fresh blood transfusion: *in cases of severe hemorrhage.*
 - Local pressure.
 - For hemathrosis: *immobilization, elastic bandage, analgesics, physiotherapy.*

	Purpura	Hemophilia
1. <i>FH</i>	Negative	Positive
2. <i>Sex</i>	Females	Males
3. <i>Age</i>	Any age	Since birth
4. <i>Relation to trauma</i>	Immediate	Delayed
5. <i>Hemarthrosis</i>	Uncommon	Common
6. <i>Hess test</i>	Positive	Negative
7. INVESTIGATIONS		
• BT • CT • APTT • Platelets	• Prolonged • Normal • Normal • Low	• Normal • Prolonged • Prolonged • Normal

Hypoprothrombinemia

ETIOLOGY

1. Liver cell failure.
2. Vitamin K deficiency: *OJ, Oral anticoagulants, Malabsorption syndrome.*
3. Hereditary deficiency of prothrombin: RARE.

CLINICAL PRESENTATION

- Bleeding tendency: especially *post-traumatic*.
- CP of the cause: most important features of each cause.
e.g. Features of liver cell failure.

INVESTIGATIONS

1. APTT is prolonged.
2. PT is prolonged & improves by parenteral vitamin K *in cases of vitamin K deficiency ONLY*.
PT is prolonged but does not improve by parenteral vitamin K *in cases of liver cell failure*.
3. TT is normal.
4. Investigations for the cause: most important investigations of each cause.
e.g. Hypoalbuminemia in liver cell failure.

TREATMENT

1. Transfusion of: *fresh frozen plasma.*
2. Treatment of: *the cause:* e.g. ttt of liver cell failure.
3. Treatment with: parenteral vitamin K *in cases of vitamin K deficiency.*

HENOCH-SCHONLEIN PURPURA

ETIOLOGY

- It usually follows a: STREPTOCOCCAL INFECTION.
- It usually affects: CHILDREN.

CLINICAL PICTURE

1. Blood: Purpura.
2. Joints: Arthralgias.
3. GIT: Abdominal colics, Melena, Hematochezia.
4. Renal: Hematuria, GN, Renal failure.

TREATMENT

- Corticosteroids: prednisone 1 mg / Kg / day orally.

THROMBOCYTOSIS



1. ESSENTIAL THROMBOCYTOSIS " PRIMARY "

- A) It is a myeloproliferative disorder (Blood malignancy) characterized by:
 " Excessive proliferation of "

MEGAKARYOCYTES in BM → ↑↑ Platelets in the peripheral blood.

- B) It also occurs in other forms of MPD: CML, PRV, *Idiopathic myelofibrosis.*

CLINICAL PICTURE

1. THROMBOSIS.
2. BLEEDING.
3. SPLENOMEGALY: HUGE size.

INVESTIGATIONS

1. Platelet count: persistently greater than 1,000,000 / cmm.
2. Bone marrow: marked Hypercellularity of Megakaryocytes.

TREATMENT

1. Chemotherapy: Hydroxyurea, Radioactive phosphorus.
2. Symptomatic ttt: Platelet-pheresis.

2. **REACTIVE THROMBOCYTOSIS** " SECONDARY "

- It is more common than essential thrombocytosis.
- Causes include:
 - *Inflammation.*
 - *Infection.*
 - *Malignancy.*
 - *Hemorrhage.*
 - *POST – SPLENECTOMY.*

THROMBOPHILIA (Hypercoagulability)

Thrombophilia is the tendency to develop thrombosis (blood clots) due to an abnormality in the system of coagulation.

CAUSES

I. Congenital:

- Homocysteinemia.
- Factor V Leiden.
- Prothrombin mutation.
- Deficiency of: protein C, protein S, Antithrombin III.

II. Acquired:

- Homocysteinemia.
- Antiphospholipid syndrome.
- SLE.
- PNH.
- DIC.
- Myeloproliferative disorders.
- Malignancy.
- Nephrotic syndrome.
- IATROGENIC:
 - CCPs.
 - Heparin – induced thrombocytopenia.

DISSEMINATED INTRAVASCULAR COAGULATION DIC

DEFINITION

- Abnormal activation of coagulation → excessive THROMBOSIS in the circulation.
- CONSUMPTION of platelets & clotting factors occurs.
- Thrombosis → secondary activation of Fibrinolysis → ↑ FDPs → excessive BLEEDING.

ETIOLOGY

1. Septicemia.
2. Severe: shock, burns, trauma.
3. Severe: hemolytic transfusion reactions.
4. **Advanced** obstetric complications: abruptio placenta, eclampsia.
5. **Advanced** malignancy.

CLINICAL PICTURE

1. Extensive BLEEDING.
2. Associated Multiple organ failure: ARF, ARDS, SEPSIS.
3. Associated Hemolytic anemia: microangiopathic.
4. THROMBOTIC events: especially skin & kidneys.

INVESTIGATIONS

1. BT, CT, PT, APTT, TT: prolonged.
2. Platelet count: decreased.
3. Fibrinogen level: decreased markedly.
4. FDPs: HIGH LEVELS.

TREATMENT

1. TTT of the cause.
2. For BLEEDING: Platelet transfusion, Fresh frozen plasma.
3. For THROMBOSIS: Heparin may be used to prevent intravascular clotting.

CAUSES OF SPLENOMEGALY

I. INFECTIONS

1. Viral: *IMN, HIV, Viral hepatitis.*

2. Bacterial:

- SBE.
- Septicemia.
- Brucellosis.
- Typhoid.
- TB: *Miliary TB.*

3. Parasitic:

- Malaria.
- Schistosomiasis.
- Toxoplasmosis.
- Kala-azar.

4. Mycoplasma, Fungi, Rickettsiae.

II. CONGESTIVE SPLENOMEGALY

1. All causes of portal hypertension.
2. Splenic vein occlusion.

III. HEMATOLOGIC

1. Anemias: *Hemolytic, megaloblastic, iron deficiency.*
2. Immune cytopenias: *AIHA.*
3. Blood malignancies: *Leukemias, Lymphomas, MPD.*

IV. NEOPLASTIC

1. Blood malignancies.
2. Primary splenic tumours: *Lymphangiosarcoma.*

V. INFILTRATION

1. Lipid storage diseases.
2. Amyloidosis.

VI. INFLAMMATION

1. Collagen diseases: *SLE, Felty's syndrome, Still's disease.*
2. Sarcoidosis.

VII. ENDOCRINE

1. Acromegaly.
2. Grave's disease.

VIII. SPLENIC ABSCESS & CYST.

CAUSES OF HUGE SPLENOMEGALY

1. Severe portal hypertension: *especially Schistosomiasis.*
2. Infections: *Chronic malaria, Kala-azar.*
3. Hematologic: *Thalassemia major.*
4. MPD: *CML, PRV, Essential thrombocythemia, Idiopathic Myelofibrosis.*
5. Neoplastic: *Lymphomas, Hairy cell leukemia.*
6. Infiltration: *Amyloidosis, Gaucher's disease.*
7. Inflammation: *Sarcoidosis, Felty's syndrome.*

HYPERSPLENISM

DEFINITION

- Exaggeration of the normal splenic function → destruction of one or more of the blood cells:
“Monocytopenia, or Bicytopenia, or Pancytopenia”.

ETIOLOGY

1. Secondary: Splenomegaly.
2. Idiopathic: Rare.

CLINICAL PICTURE

1. One or more of the following:
 - Anemia: RBCs.
 - Bleeding: PLATELETS.
 - Fever & recurrent infections: WBCs.
2. Splenomegaly: + features of the cause of splenomegaly.

INVESTIGATIONS

1. **CBC**: One or more of the following:
 - RBCs: Normocytic normochromic anemia, with reticulocytosis.
 - PLATELETS: Thrombocytopenia.
 - WBCs: Leukopenia.
2. **Bone marrow examination**: Hyperplasia.
3. **Cr. Labeled RBCs**: excessive destruction in the spleen.
4. **Investigations for the cause of splenomegaly**.

TREATMENT

1. SPLENECTOMY.
2. Symptomatic ttt: *for anemia, bleeding, infections.*
3. TTT of the cause.

LYMPHOMAS

DEFINITION

- Neoplasms of the IMMUNE SYSTEM (**B or T lymphocytes**) usually arising in the LN.
- They are classified according to HISTOLOGY into:
 - Hodgkin's disease (HD).
 - Non-Hodgkin's lymphoma (NHL).

ETIOLOGY

1. The Rule: UNKNOWN.
2. The Exception: associated with: **I**nfection (EBV), **I**rradiation, **I**mmunodeficiency.

CLINICAL PICTURE

I. LYMPHATIC MANIFESTATIONS

1. LYMPHADENOPATHY

A. LN ENLARGEMENT

- In HD: **Discrete**, rubbery, painless, nontender.
Localized at the onset, then become generalized.
- In NHL: **Amalgamated**, rubbery, painless, nontender.
Generalized at the onset.

B. PRESSURE MANIFESTATIONS

- Mediastinal syndrome, Obstructive jaundice.

2. SPLENOMEGALY

- May reach a **HUGE** size.

II. EXTRA-LYMPHATIC MANIFESTATIONS

1. GENERAL

- **F**ever: "Pel-Ebstein in HD"
Fever for 1-2 weeks alternating with No fever for 1-2 weeks.
- **F**atigue: + loss of weight + night sweats.

2. ABDOMINAL

- Liver: Hepatomegaly & jaundice.
- GIT: Bleeding & malabsorption.

3. CHEST

- Lung: Infiltration.
- Pleura: Effusion.

4. NEUROLOGICAL

- Focal spinal manifestations: *e.g. paraplegia.*
- Focal cerebral manifestations: *e.g. hemiplegia.*

5. SKIN

- Pruritus.
- Nodules.
- Hyperpigmentation.

6. SKELETAL

- **P**ains: bony.
- **P**athological fractures.

7. IMMUNOLOGICAL

- Immunodeficiency → Opportunistic infections: HZ, Fungi.
- Immune cytopenias → AIHA, Autoimmune thrombocytopenia.

INVESTIGATIONS

1. **BIOPSY** (LN, BM)

“ The most important investigation ”

- In HD: The histological hallmark is: “ Reed Sterberg cell ”.
- In HD: The histological classification is: “ 4 types ”:
 - *Lymphocyte predominance:* *many Lymphocytes, few RS cells.*
 - *Lymphocyte depletion:* *few Lymphocytes, many RS cells.*
 - *Mixed cellularity.*
 - *Nodular sclerosis:* *excessive fibrosis.*

2. **BLOOD PICTURE**

- WBCs: Leukocytosis, Lymphocytosis.
- RBCs: Anemia (AIHA or Myelophthisic).
- PLATELETS: Thrombocytopenia (Autoimmune).
- ESR: Elevated.

3. **IMAGING**

- ABDOMEN: Abdominal ultrasonography & CT.
- CHEST: CXR & CT.

4. **STAGING LAPAROTOMY.**

CLINICAL STAGING OF LYMPHOMAS

- I. Single LN region or Single extralymphatic site.
- II. Two or more LN regions on the **same side** of the diaphragm.
- III. LN regions on **both sides** of the diaphragm.
- IV. Diffuse extralymphatic sites.

A = **A**bsence of systemic symptoms.

B = **P**resence of systemic symptoms (*fever, weight loss, night sweats*).

TREATMENT

1. RADIOTHERAPY

- Stages: I or II A.
- Severe pressure manifestations: e.g. focal spinal cord compression.

2. CHEMOTHERAPY

- Stages: II B, III, IV.

In HD: **MOPP** (**M**echlorethamine, **O**ncovin, **P**rocarbazine, **P**rednisone).

In NHL: Cyclophosphamide, Doxorubicin, Oncovin, Prednisone.

GENERALIZED LYMPHADENOPATHY

INFECTIONS

1. VIRAL: IMN, AIDS, Viral hepatitis.
2. BACTERIAL: Brucellosis, TB, Secondary Syphilis.
3. PROTOZOAL: Toxoplasmosis.
4. FUNGAL: Histoplasmosis.

NEOPLASTIC

1. BLOOD MALIGNANCIES: Lymphomas, Leukemias, MM.
2. SOLID MALIGNANCIES: Metastatic carcinoma.

IMMUNOLOGICAL

1. SLE, Felty's syndrome.
2. SARCOIDOSIS.

METABOLIC

1. AMYLOIDOSIS.
2. LIPID STORAGE DISEASES.

رقم الإيداع: ٢٤٤٠٥ / ٢٠٠٨

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